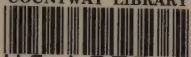


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VOL. XXV

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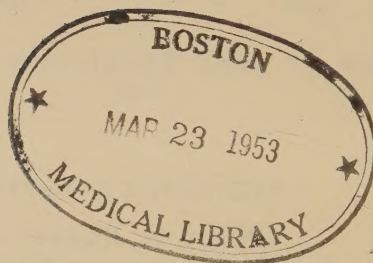
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Mr. McNamee

IN MEMORIAM PROF. DR. B. BROUWER

On November 1st, 1949, Prof. Dr. Bernardus Brouwer died unexpectedly in Amsterdam in the middle of his work, as if struck by lightning. On November 5th he was laid to rest in the presence of a vast multitude of sympathizers. The coffin containing the mortal remains was carried to the grave by 12 of his former assistants—a touching symbol of how greatly his pupils feel indebted to him. With him a great neurologist, a good, warm—feeling, and cordial man, an excellent organiser and a man of eminent didactic qualities is gone for ever.

Prof. Brouwer was born in Amsterdam on March 23th, 1881 and studied medicine at the University of Amsterdam, where he qualified on December 17th, 1906. On March 12th, 1909, he acquired the degree of doctor of medicine with Prof. Winkler, on a thesis called: *Deafmutism and the Acoustic Tracts*.

It was in 1912, with his appointment to the post of sub-director of the Central Institute for Brain-Research, that his actual career as a scientific neurologist began. In 1920 he was the first to be awarded the gold Ramaer-Medal by the Dutch Society for Psychiatry and Neurology. In 1923 followed his appointment to the post of professor of Neurology, as the successor of Prof. Wertheim Salomonson, upon which office he entered by delivering a lecture on *The Autonomic Nervous System and Feeling*. In 1926 he was elected a member of the Royal Dutch Academy of Sciences.

Whereas at first his clinic remained situated in the “Binnengasthuis”, where he was forced to do his scientific research-work under primitive conditions, a few years later the building of a new institute in the “Wilhelmina-Gasthuis” was started, which was afterwards festively inaugurated on September 23rd, 1929. The foundation of this new clinic, with a neurosurgical department and extensive laboratories of its own, was not only a milestone in Prof. Brouwer’s life, but in the history of Dutch neurology as well. It is he, indeed, who, although not a surgeon himself, has introduced the surgery of the nervous

system as a separate specialism in the Netherlands. In doing so he achieved a pioneer's act, which has proved to be of beneficial and far-reaching importance. The way in which an idea was here realized, in spite of the numerous difficulties that were in his way, was characteristic of the iron energy and methodical tenacity of Prof. Brouwer's, who was provoked to fresh activity by every obstacle and who did not shrink from problems, in order to reach this one eventual purpose: of gaining, in whatever way, a better treatment for the Dutch neuro-surgical patient. And any expert will testify that he fully succeeded.

In 1938 his work was interrupted for months by a chronic disease. Twice he was subjected to a major operation and scarcely escaped death. A long period of convalescence was at last followed by complete recovery.

In 1940, the year in which the war broke out, Prof. Brouwer was called upon to occupy the then so very difficult office of vice-chancellor of the University of Amsterdam, which he held for two successive years. His management in these years provoked a great deal of criticism from various quarters. No wise man who is fairly abreast of the whirlpool of events into which the University was then hurled will be inclined to deny that here a patriotic man stood continually in the breach for the welfare of the University in accordance with his own view of affairs and he consequently carried through his own policy and stood firm for his personal opinion and never disavowed it, not even in a subsequent phase when this might have been of great profit to him.

On April 1st 1946, he was, without his own request, honourably discharged as professor. A more serious blow could hardly have struck him, attached as he felt to the University, his university post and his clinic. He has borne this grief, not with resignation, but with a revolting and ever efficient spirit.

It is a remarkable coincidence that a few months later in the same year Prof. Ariens Kappers suddenly died, the post of director of the Central Institute for Brain-Research thus falling vacant. In the opinion of a great many, Prof. Brouwer, notwithstanding his age of 65, was the only one person to fill this vacancy in the right way and to continue worthily the illustrious tradition of the Institute, made world-famous by Prof. Ariens Kappers. He was offered this post and, accepting it, once again set to work with his traditional energy and activity. His nature and scientific training necessitated the accent of the researchwork of this institute to be shifted from comparative-anatomical to experimental and pathologic-anatomical research. That such a devel-

opment would require a great deal of energy from its leader, is evident. The annual reports of the Institute for Brain-Research for the last 3 years show what immense activity was developed by its new director, assisted by a multitude of research-workers, whom Prof. Brouwer in a very short time succeeded in surrounding himself with in his new function.

Prof. Brouwer's scientific work has been laid down in more than 240 publications. All his writings and lectures were thoroughly prepared, well-founded, worked out in detail and fully illustrated. They reveal their author as a keen observer, an exemplary morphologist, a high-class clinician and a prudent therapist. He always tries to find and repeatedly does find the main lines that lie hidden in any pathological event. His thought is not brilliant and flashing, but rather gradual and methodical and based upon the facts which he subjects to a systematic and thorough investigation and forms into original groups.

His style is simple and naïve, in the English sense of the word, as Kinnier Wilson once said of him. He was not a book-worm, but a research-worker dressed in white laboratory-uniform, who, bent over his microscope, made notes of his experiences and laid them down in simple but exact sketches.

A long series of his innumerable anatomical as well as clinic contributions will survive as lasting acquisitions of science. Decidedly classic should be called his work on *The Projection of the Retina in the Brain*, partly in collaboration with Prof. W. P. C. Zeeman, M. D. The coupling of two experimental series with rabbit and monkey—on the one hand the fixing of secondary degeneration in the corpus geniculatum externum by local lesions of the retina; on the other hand the fixing of retrograde degeneration in the same ganglion by local lesions of the area striata—enabled him to make an accurate statement of the localisation of the various retina-quadrants in the entire optic system. It particularly appeared here that the macular fibres occupy a large area in this system and that especially the macular projection on the occipital cortex covers an extensive space, which, also supported by clinico-anatomical experiences of other research-workers, can be stated with sufficient accuracy, also in man.

In a subsequent phase of this wide optic research it moreover appeared that, just as it had been proved by others before in the rabbit, there must also exist in the monkey a corticofugal connection from the area striata back to the corpus geniculatum, and in all probability also in man. It is probable, as Brouwer writes, that on account of this the psychological mechanism of attention can be given a physiologico-anatomical basis.

Besides the optic system a series of experiments was devoted to the structure of the *cerebellum*. In connection with the work of Edinger on palaeo- and neo-cerebellum, Brouwer succeeded in marking off an old and a new part also in the inferior olivary system. He moreover found new observations about hemiatrophia neocerebellaris, which together with van Valkenburg's findings on the myelinisation of the cortex of the cerebellum, gave another foundation to Edinger's thesis. This phylogenetic distinction in the younger and the older parts of the nervous system occupied Prof. Brouwer for years and so did particularly the gradually growing experience that the younger parts are of a greater vulnerability to pathological processes.

This has been the leading thought in many of his clinico-anatomical contributions. In his experiments on sensibility he describes the phylogenetic development of the posterior columns, the conductor of gnostic or neosensibility and convincingly points out the excessive vulnerability of this part of the spinal cord. We come across the same principle when it is explained to us why the temporal, non-crossing fibres of the optic nerve degenerate sooner in sclerosis multiplex than the nasal ones do, why the pyramidal tracts react so early upon various injurious agents and why particularly the abdominal reflexes are so very early abolished, in the case of pyramidal lesions.

It was finally along a purely phylogenetic way that Prof. Brouwer came to an exact description of the oculomotorial nucleus which has been universally accepted in international literature.

He was greatly interested in the relations of the *dermatomes*, to which subject several of his earlier publications are devoted. In this his work was chiefly based on that of Bolk, whose schemes he kept using in his clinic, even at the time when the larger dermatomes of Foerster's gradually began to supplant those of Bolk's. In an exemplary way Prof. Brouwer proved that the pseudo-hysterical glove- and sock-shaped anesthesia, as they are occasionally found in syringomyelia, can be simply accounted for, if it should be accepted that various parts of a dermatome are being projected on various cells of the posterior horn.

Also in the domain of endogenic diseases did Prof. Brouwer yield original contributions. I refer here particularly to the mixture of *Tabes of Friedreich and sclerosis multiplex* as described by him with anatomic verification in 1920. In doing so he was two years ahead of Mondini, who published an analogical observation in 1922. He published other similar cases in 1933 and 1939, emphasizing the desirability that in future more attention should be paid to the endogenic factors which undoubtedly, among others, play an important part in the still mysterious etiology of sclerosis multiplex.

Of late years Prof. Brouwer chiefly occupied himself with studies on the *hypothalamus*. In the Amsterdam Neurological Society he introduced a series of eight cases, all of them clinically observed and anatomically veriflicated, in which the endocrinological syndrome was confronted with the anatomic lesion, the limitation of which could be accurately stated by means of an analysis in serial sections, a form of analysis which, up till then, had not yet been attempted in this domain. In this analysis it became evident that more than once a certain localised focal process does not give rise to the symptoms which, considering the localisation, might be expected, and that apparently a great deal depends on the nature of the process and the rate at which it develops. That is why, as the author puts it, both positive and negative aspects can be pointed out in the pathology of the hypothalamus, apparently largely dependent on the possibility of an effective compensating mechanism occurring in an affected brain.

Prof. Brouwer was possessed of a unique energy and a talent, all his own, to divide the time available as methodically and justly as possible between his numerous and various duties. Besides that he was utterly punctual, always promptly in time and in the habit of answering his vast correspondence by return of post with short and plain letters, the distinctness of which left nothing to be desired.

There is no doubt that he influenced all those who used to work, in whatever function, under, next to, or with him, in a powerful and stimulating way. All of those who in the course of years worked under his direction, were again and again struck by the pushing and suggestive influence that was radiated by his enthusiastic, nearly always cheerful, and good-natured personality. The atmosphere which he, in a most natural way, succeeded in creating about him, was warm and humane and vibrating with high-spirited activity. Small wonder that in this way he knew how to stimulate his assistants to a complete development of their energy, to lift them above the daily routine of their clinical work and to urge them to research of their own, at the same time paying careful attention to the personal characteristics of each of them. Is it small wonder then that in doing so he achieved, so to say, to bring out the best in these young people?

Prof. Brouwer was an eminent physician in the general sense of the word. His wide interest, not only in the complaints, but also in other needs of his patient, made him a highly humane physician, from whom a countless multitude was so fortunate as to receive aid and support during a large number of years and in a most variegated selection of problems. In spite of his choice of therapeutics being very simple and his knowledge of specialities very limited, his sugges-

tive influence over his patients was often so great, that he managed to keep a great many chronic patients in balance for years at a stretch.

Moreover, he was a supreme neurological clinician, not, however, in the first place due to the quality of his examination. The latter was effective, but simple, delicate technical tricks not being in his line and he only rarely applying them. He used to stick to the same, uncomplicated scheme of examining to which he had been used for years. For the value of a certain symptom he had, however, an almost infallible feeling. In the interpretation of the anamnesis, the grouping of the symptoms, and the construction of his diagnosis he was a veritable master indeed. The continual checking-up of the clinical diagnosis he considered of the greatest importance, either by means of an after-examination, an operation or a post-mortem examination. The joint sessions with the pathologist around the stone section-table were one of the monthly red-letter days in the clinical proceedings. Woe him who had sent a patient, dying of tumor cerebri, to the pathologist with the diagnosis of thrombosis cerebri!

Let us not forget, in our attempt to reveal all these aspects of Prof. Brouwer's personality, that he was highly interested, not only in science as such, but in literature and history as well and especially in music. He had a marked gift for music, used to attend the concerts in the Amsterdam Concertgebouw regularly and sometimes pondered on the compositorial problems of certain symphonic creations.

Boundless was, indeed, the hospitality in his stately mansion on one of the Amsterdam canals, in the heart of his beloved native town. Many a time it has been a meeting-place of prominent personalities of international science, more often, however, did he gather his assistants and pupils around his ever well-provided table. In an exemplary way Mrs. Brouwer used to assist her husband in his comprehensive task during the forty years of their married life and to share with him all the happiness and sorrows of his rich life.

A great neurologist and a good man is gone for ever.

A. Biemond,
Wilhelmina-Gasthuis, Amsterdam.

INTRADURAL LIPOMA OF THE SPINAL CORD

By

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Barcelona (Spain)

The intradural lipomas of the spinal cord are uncommon. Cases have, however, been described by several authors. These were analysed in the papers by *Guillain, Bertrand and Salles* (1937) (12), *Jabotinski* (1939) (14), *Bucy and Gustafson* (1939) (5), and in the most recent work of *Ehni and Love* (1945) (8), in which 29 cases of this tumoral type are compiled, analyzed and compared. In 1944 *Ehni and Pugh* (7) published the first case in which the pathological diagnosis was made before the operation. To these cases we have to add four others reported by *Robineau* in 1932 (17) (one case of his own, two of *Vincent's*, and another of *de Martel's*), together with the one which constitutes our own contribution in this paper.

Altogether there are 35 cases of intradural intraspinal lipoma where a symptomatological analysis is possible. Other cases have been simply tabulated in general statistics.

CASE REPORT

R. M. E. , a man 21 years old, unmarried, was first seen by us on April 19, 1948. Our diagnosis was spinal compression and we accordingly recommended his admission to the "Neurosurgical Service" of the "*Instituto Policlinico*" under the care of Dr. Tolosa.

Family History: without interest.

The patient was born in absolutely normal conditions, he began to talk and walk at the normal time; right handed; when 15 years old he suffered from a pleurisy, from which he recovered.

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Present Illness.

Four months before consulting us the patient began to feel a sensation of weakness and premature fatigue, followed a few days afterwards by *tactile hypesthesia* and *acroparesthesias* in the toes of the right foot. In the course of the following days he felt the same disorders in the right knee and groin, and about a fortnight later also in the left lower limb. From that time he felt a *general hypesthesia below the umbilical line*. In the beginning of this illness he experienced a certain difficulty with micurition (which later on disappeared), and fecal retention or constipation, which still persists. There was also sexual impotence.

Not long after the sensory disorders appeared in the lower limbs both legs became weak. This weakness has increased to the extent that for a month now he has been obliged to lie in bed, and there have been periods of spontaneous clonus in the lower limbs.

He has not presented sensitive disorders of the radicular irritative type, and only on one occasion, in the course of development, did he suffer pain at the level of the left lumbar region.

Clinical Examination.

Spastic paraparesis with ataxic-spasmodic gait; the ataxic component was very remarkable. Strong spastic hypertonia. The Barré sign is positive on both sides. *Knee and ankle jerks hyperactive*. *Clonus* on both knees and ankles. *Babinski's sign* on both sides. On the right leg reflexes of spinal automatism may be detected.

Cremasteric reflexes are abolished. The upper abdominal reflexes are abolished, and the middle and lower ones are brisk.

Sensitivity: on the right side there is a hypesthesia starting at the level of the seventh dorsal dermatoma; it becomes intenser the lower it goes. On the right lower limb there is an almost absolute *anesthesia*. On the left side there is a band of strong hypesthesia from the seventh dorsal dermatoma up to the tenth or eleventh one, which is attenuated on the lower dermatomas. *The sensitive disorders affect all modalities*: superficial contact, cold, heat, pain, notion of position and vibration.

The painful stimuli on the left lower limb are felt as "cold".

Plain X-ray of spine found not spondylitis.

On April 20, 1948, a lumbar puncture and manometric tests were made, showing a *total blocking* of the subarachnoidal spaces. 10 cc. of a yellowish fluid were extracted. The analysis of this fluid showed 1,70 grs. per thousand of albumina, 1 cellule per cubic milimeter, and Pandy's reaction was positive.

On April 20, 1948, a cisternal injection of 3 cc. of heavy lipiodol were made. In a radiography taken 24 hours later we observed that the *lipiodol shadow was stopped at the level of the third dorsal vertebra*, there taking the form of a *broad dome*, and thence spreading downwards around the angles the length of two vertebral bodies.

On the following days there appeared some thoracic paresthesia of a constrictive type.

The clinical diagnosis was: *upper thoracic spinal compression, probably by intraspinal tumour*.

The patient was operated upon on April 26, 1948. Under intratracheal ether anesthesia a laminectomy was performed from the third to the ninth thoracic vertebra. The spinal canal as filled by an asimetrically enlarged and tense dural

sac which did not pulsate. On opening the dura a *voluminous growth of a yellowish colour* was found which filled the whole spinal canal. The tumour was located *under the pia-arachnoid* and was *firmly attached to the cord*. There was no line of demarcation between the tumour and the spinal cord, which was obviously invaded by the tumoral tissue. The leptomeninges were opened and strips of tumor were cut by sharp dissection from the posterior surface of the cord. The vascularization of the tumoral tissue was poor. The *removal of strips* continued until the vicinity of the cord was reached. A layer of tumoral tissue was left over the cord to avoid damaging the latter. The lateral surfaces of the spinal cord also showed a yellowish discoloration which suggested that the tissue growth extended around it. The dura mater was closed tightly and the muscles and skin were sutured by layers.

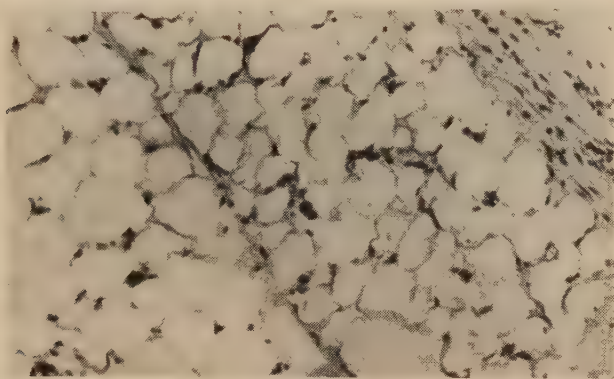


Fig. 1.

The histological examination of the tumoral tissue showed "lipomatose lobules separated by small connecting links. The surface of this nodule is covered by a conjunctive membrane with a mild inflammatory reaction. *Lipoma*" (fig. 1).

Postoperative course:

The patient experienced a slowly *progressing improvement*.

An examination performed twelve days after the operation (on May 8), showed:

Spastic paraparesis with spontaneous clonus on both knee and ankles. The voluntary motility was limited to incomplete movements of knee, hip, and toes. Babinski's sign.

Three months after the operation the patient walked normally and goes up and downstairs without a stick. Four months later he can walk *about as long as he likes, does normal work and he even runs and dances well*. This state during actually.

During the post-operative course we had occasion to show the patient to Professor *Ludo van Bogaert*, (4) who, having become interested in our observation, called our attention to the patient's "*piéd creux*" on the left side, and also to the morphology of his thorax (fig. 2). The patient's father, upon being questioned about these points, said that the "creux" in his son's foot had been the same throughout his life. These signs must undoubtedly be understood, as suggested by *van Bogaert*, as belonging to a *dysraphicus condition*.



Fig. 2.

COMMENTS

Looking over the previously reported cases of spinal cord lipoma we were impressed by the symptomatological resemblance observed between our present case and that described by *Ehni* (7, 8).

The more outstanding findings in our case were:

- (1) A *syndrome of the posterior columns* with *ataxia* and *defects of the deep sensibilities*.
- (2) *Absence of radicular pains*.
- (3) *A widening of the spinal canal*.

During the immediate post-operative course, the patient recovered first the superficial sensibility, while the arthrokinetic and vibratory disturbances persisted further.

An X-ray of the lumbosacral region did not reveal spina bifida.

Clinically we also with the syndrome of posterior columns found the classical irritative pyramidal syndrome of spinal compression.

The "pied creux" of our patient suggested the relation of these growths with the *status dysraphicus*. *Ehni* and *Pugh's* (7) observations with "café au lait" cutaneous stains renews the connection of the lipomas with neurofibromatosis, although to this day such connections cannot be set down as certain. Another fact to be taken into account to

complete the characteristics of these central nervous system lipomas is their frequently diffuse character, as remarked by *Baker and Adams* (1938) (3).

The clinical syndrome of the intradural lipomas such as *Ehni* has pointed out (8) may be difficult to differentiate from the *teratomas* or *mixed tumors of the spinal canal*. According to *French and Peyton* (1942) (10) the latter are characterized specially by a fusiform enlargement of the spinal canal and a slow evolution of the symptoms. This slow development may be missed in the intradural lipomas, as for instance in our case, in which the development took only four months. On the other hand, mixed tumors usually appear in children and young people, while lipomas also affect adults. Besides, mixed tumors, according to *French and Peyton*, are accompanied by spina bifida. *Ingraham and O. Bailey* (1946) (13) have demonstrated the histological relations between teratomas and lipomas.

The *intradural epidermoid syndrome*, as observed and described by *Almeida Lima* (1943) (15), with rather intense participation of posterior columns without radicular pains, might clinically resemble that of *Ehni* (8) as typical of the intradural lipomas. However, in an observation of epidermoid made by ourselves the radicular pains had the same intensity and development as in a case of neurinoma (1948) (2).

Other ataxic syndromes due to spinal compression have been described in other tumoral types by *Elsberg* (1925) (9), *Guillain, Bertrand and Garcin* (1930) (11), *Neri* (1932) (16), *Alajouanine* (1932) (1), *Decourt and Petit-Dutaillis* (1933) (6), and *Rouquès, David and Paukrat* (1946) (18). In the case of *Petit-Dutaillis* there were no radicular pains, it was a case of thoracic meningioma in anterolateral position. The case of *Rouquès* and his associates (18) was very interesting; clinically it offered the following characteristics: weakness of the lower limbs, Babinski's sign on both sides, exaltation of the ankle jerk, obvious hypotonia with broad extensibility and exaggerated passivity on both sides, slight disturbances of superficial sensibility, deep sensibility absolutely lost, tabetic walk, and Romberg sign strongly positive. There were no sphincter disturbances. This is the most complete and almost exclusive clinical syndrome of posterior columns produced by tumoral spinal compression that has come to our knowledge. It was an extraspinal subarachnoidal glioma at TII-LI, which was extirpated. The patient was young woman twenty-one years old.

These cases of ataxic symptomatology due to spinal cord compression not produced by lipoma do not destroy *Ehni's* conclusions, although they help to limit their true value. Our case confirms, in

accordance with the opinion of the authors of Mayo Clinic, that when a spinal compression is observed with *predominant or exclusive syndrome of the posterior columns, without radicular pains and widening of the spinal canal*, and particularly if the *clinical evolution* has been *slow*, it is to be suspected that there exists an *intradural lipoma*. If with the help of lipiodol or in some other way it can be demonstrated that the *tumour is rather long*, this will have more probabilities of being the correct conclusion.

In our case, fortunately, the *subtotal removal* of the growth did not affect the blood supply of the spinal cord, contrary to observations made by *Ehni and Pugh* (7) in their case. We were therefore able to carry out the rather considerable removal followed by a very satisfactory postoperative development and complete recovery of the patient,

TABLE

N	Year	Author	Sex	Age at onset of Symptoms	Duration	Level	Position on Cord	Traversing Roots
30	1932	Robineau ¹⁷	M	39 yr.	1 yr.	thoracic inferior	right posterior	
31	1932	Cl. Vincent ¹⁷	M	16 yr.	12 yr.	cervico-thoracic	posterior	
32	1932	Cl. Vincent ¹⁷	F	4 yr.	10 yr.	cervico-thoracic	posterior	

The results obtained by other authors, e.g. *Bucy* and *Gustafson* (5), and ourselves, is to suggest in all cases the subtotal removal if the spinal cord or its blood supply is not injured. The long results are relatively favourable because of the slow growth of the tumour.

However, in Case I of the series of the Mayo Clinic the growth relapsed clinically after nine years. When no other means are adequate the surface of the growth must be cut and the dura left open.

We deem it of interest to present in the following table the characteristics of the cases of *Robineau* (17), *Vincent* (17), *de Martel* (17), *Ehni* and *Pugh* (7), and ours, following the pattern and numbers of *Ehni* and *Love* (8).

De Martel's case is the only one known of Intradural Lipoma of the spinal cord of prespinal position.

Data on Cases of Intradural Lipoma following that of Ehni and Love⁸

Connective Tissue	Spinal Puncture	Roentgenographic Evidence	Other Disorders	Operation
pure Lipoma. spinal cord infiltration				Removal of the pieces with the scoop. The patient improves. Six months later he remains in the same good state.
was impossible separate the growth from spinal cord.	Albumino-citological dissociation Total block.	The Lipiodol stops at the T ₂ and forms dome's shape.		Partial removal with the scoop from the C ₇ to the T ₄ . During the operation examined the patients reactions in order to avoid the daimage of the spinal cord. A year latter the patient's gait had improved.
was impossible divide the growth from the spinal cord.	Albumino-citological dissociation Total block.			Partial removed with the scissors. Slight improvement. Two months latter the patient goes worse. A second operation is performed. Subtotal removal. Slight improvement.

N	Year	Author	Sex	Age of onset of Symptoms	Duration	Level	Position on Cord	Traversing Roots
33	1932	De Martel ¹⁷	M	23 yr.	10 yr.	thoracic superior	anterior and chiefly left	
34	1944	Ehni and Pugh ¹⁷	M	40 yr.	7 months	T ₆ -T ₁₁	left posterior	posterior roots pass through tumour
35	1948	Barraquer-Ferré, Tolosa, Barraquer-Bordas, and Durán	M	21 yr.	4 months	T ₃ -T ₉	posterior	posterior roots pass through tumour

Connective Tissue	Spinal Puncture	Roentgenographic Evidence	Other Disorders	Operation
was possible separate the tumour by both sides, but he the anterior part the growth made a total block with the spinal cord.		Arrest of the ascending lipiodol at T₄.		Removal of the growth. After two years no improvement is noted. A second operation is performed. It is found a cystic excavation in the spinal cord. No improvement.
It tissue with small amount fibrous stroma. capsule of heterogeneous connective tissue.	The protein are increased in c.s.f. Strong block.	Obstruction of iodized oil ascending at the tenth thoracic interspace. Partial wedging of the body of the eighth thoracic vertebrae and suspicious widening of the spinal canal through the fifth and sixth thoracic vertebrae.	Cofé au lait spot in the right loin.	The removal of the growth was not possible because the blood supply of the spinal cord might be damaged. The capsule of the tumour was incised and the incision in the dura was left open. Beginning to appreciate motion in his large toe when the patient was dismissed.
Masses of lipoma-like tissue, are separated by connective stroma. Connective capsula. It was impossible separate the growth from the tumour. The sides of the spinal cord offer a brownish colour.	Albumino-citological dissociation. Total block.	Widening of the spinal canal. Arrest of the descending lipiodol at T₂.	Left "pied creux". Abnormal morphological thorax. (Status dysraphicus).	Subtotal removal with the scalpel. After almost two years a great improvement is maintained.

SUMMARY

1. The authors present a personal observation of intradural lipoma of the spinal cord in a 21 year old male. The clinical picture was characterized by a *syndrome of the posterior columns, absence of root pains and widening of the spinal canal*. There existed a *spastic paraparesia* and a *sensitive level*. There was *albuminocitological dissociation, manometric block and arrest of descending lipiodol*. The patient had a "*pied creux*" and *morphologically abnormal thorax*. The surgical *subtotal extirpation* brought a *good recovery*.

2. The authors discuss the diagnoses of intradural lipomas and mixed tumors, epidermoids and spinal compressions of ataxic type.

3. They refer also to the cases of *Robineau* (17), *Vincent* (17), *de Martel* (17), and *Ehni* and *Pugh* (7), which are added to the analytical table published by *Ehni* and *Love* (8).

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SUPRAVITAL ANALYSIS OF DISORDERS IN THE CEREBROVASCULAR PERMEABILITY

III. A Critical Analysis of the Technique and Results Obtained in Experimental Animals.

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Previous investigations of disorders in the permeability of the cerebral vessels showed that a disorder in experimental animals could be visualized by means of a colour indicator, not only *intra vitam* but also a short time after the death of such an animal (*Broman* 1938, 1940). This disclosure cleared the way for the examination of the human brain, if removed very early post mortem (*Broman* 1944, 1947). This type of examination is, however, more deceptive and impaired by more sources of error than the ordinary method, in which experimental animals are injected intravitaly with dye-stuffs. A critical analysis of the actual technique with respect to possible sources of error and to the effect of agonal factors was therefore called for and prompted the present study. This analysis has been divided into two parts, viz. (a) control series of animal experiments (reported below) and (b) different kinds of comparative control experiments carried out in connection with the supravital examination of human brains—an investigation performed with the cooperation of *S. Radner* and *L. Svanberg* which will be published in this journal.

The Principles of the Supravital Examination Method.

Trypan blue (trpb.) dissolved in a saline solution is perfused centripetally via the arteries into the brain for about five minutes under a pressure somewhat below that of the blood pressure of the animal. The dye penetrates the walls of the vessels and enters the cerebral tissue, if and where the vascular permeability is disturbed. If the vessels are then rinsed with a saline solution, the dye will remain in lesioned areas only. That the intact vessels are impermeable to trpb. even a short time post mortem was explained (*Broman*) by

the assumption that the endothelial cells of the vessels survive the individual for a brief period. For this reason the investigation has been termed 'supravital'.

INVESTIGATION RESULTS

(a) *Dye Perfusion after Different Post Mortem Intervals*

Rabbits killed under anesthesia were allowed to lie for different periods, after which a freshly filtered 0.15 p. c. solution of trpb. was perfused in a cranial direction via the thoracic aorta after the right half of the heart had been opened up to permit the free drainage of the solution thus perfused. The perfusion pressure applied was about 70 mm Hg and the actual process took about five minutes, during which about 400-500 ml was perfused. Afterwards the vessels of the brain were rinsed with about 200-300 ml saline solution and then the perfusion was finished with a similar amount of 10 p. c. formalin to fix the brain. Frozen sections of all cases were made transparent and were examined microscopically.

Results:

Exp. No.	Time post mort.	Staining	Vessels containing blood	Fixation
1	½ hour	0	0	good
2	1 „	0	0	good
3	2 „	?	+	poor
4	5 „	+	+	poor

The investigations thus showed that if the animal was allowed to lie two hours before the performance of the experiment, the blood refused to be washed away by the perfusion, probably owing to intra-vascular coagulation. This residual blood had of course an adverse effect also on the perfusion of the formalin solution and consequently impaired the fixation of the brain. The resultant faint bluishness that was then macroscopically visible could not forthwith be considered a post mortem disorder in the permeability, because a microscopic control showed that the dye had forced its way into scattered vascular branches containing blood that had not been washed out. Besides this, however, in Exp. No. 4 the dye had escaped from some vessels and spread into the surrounding tissue. This was suggestive of a disturbance in the permeability, but it might also be attributed to a defective rinsing of the dye solution from some vessels. A certain amount of the dye may therefore have passed through the walls of the vessels after fixation. The result of this experiment agrees with

what was found previously in the perfusion of human brains (*Broman* 1944).

As it seems only natural that the permeability must break down after the lapse of a certain post mortem time, this investigation was complemented by a series in which the cerebral blood vessels were rinsed with a saline solution very soon after the death of the animal and intravascular coagulation thereby prevented. After a certain post mortem interval, varying from case to case, the dye solution was perfused as in the above-mentioned experiments.

Results:

Exp. No.	Time post mort.	Staining	Fixation	Animal
1	1 hour	0	good	Cat
2	2 "	0	good	Cat
3	3 "	0	good	Rabbit
4	5 "	0	poor	Cat
5	5 "	0	poor	Rabbit

It should be mentioned that in the last two experiments the dura and the choroid plexus stained but very slightly or not at all. This, as well as the poor fixation, definitely showed that in those cases in which the experiments were not carried out until five hours after the death of the animal the cerebral vessels had become blocked. This was presumably due to an absorption by the brain tissue of the saline solution contained in the blood vessels, which, on account of the swelling of the brain, were compressed and blocked.

In order to overcome the obstacles due to a post mortem delay of the examination, the animals (rabbits) were given an injection of heparin before they were killed, it being hoped that this would prevent the intravascular coagulation as well as the absorption of intravascular solution by the brain tissue (owing to the colloid-osmotic pressure of the blood).

Results:

Exp. No.	Time post mort.	Staining	Vessels containing blood	Fixation
1	6 hours	0	0	good
2	12 "	0	0	good
3	24 "	+	(+)	good

These experiments showed that the factor obstructing a late post mortem perfusion might be eliminated by heparin. After the use of heparin all the vessels were unobstructed even after 24 hours. In all of these cases a small quantity of neutral red had been added to the

formalin solution. As a consequence all the brains also displayed a distinct rather uniform redness—a further proof that the vessels must have been open to the perfusion fluid. The finding that after 24 hours scattered patches all over the brain had turned blue was, therefore, a definite sign of a (post mortem) disturbance in the vascular permeability.

It was thus obvious that the factor preventing an ordinary examination of the permeability of the blood vessels after too long a post mortem interval was above all the coagulation of the blood, and that a post mortem derangement of the vascular permeability occurred very late.

This conclusion was also confirmed by experiments in which the dye was injected into the animal in vivo but the cerebral blood vessels not washed out before a certain post mortem interval. In the following experimental series (rabbits) this time factor was varied.

Results:

Exp. No.	Time post mort.	Fixation	Macr. stain.	Blood content of vessels
1	½ hour	good	0	0
2	1 "	"	0	0
3	1 "	"	0	slight
4	2 "	unsatisfactory	+	plentiful
5	3 "	"	+	"

From the above it will be apparent that if in animal experiments the rinsing of the blood vessels is delayed or neglected, misleading results will be obtained. If the brain stains macroscopically blue under such circumstances, a diffuse disturbance in the vascular permeability cannot be forthwith concluded, because a microscopic control will show that the dye is contained within the vessels together with the residual blood, (where its concentration in ordinary experiments is too low and where it is too adherent to the blood after fixation, to be able to pass out into the surrounding tissue in sufficient concentration to be visible).

(b) The Effect of an Inadequate Washing of the Dye Solution before the Formalin Fixation

In some experiments the formalin solution was allowed to pass through the cerebral blood vessels without the dye solution from the immediately preceding perfusion being washed out with saline solution. Also in these experiments did the brain stain macroscopically. In this case, however, a microscopic control showed that the dye had also passed through the vascular walls and penetrated into the cerebral tissues. In view of the fact that the formalin solution naturally

has an injurious effect on the permeability of the vessels and thereby renders an escape of the dye possible, this result was only to be expected.

(c) Effect of Post Mortem Injury of the Brain

In order to find out the effect of a post mortem mechanical lesion of the brain prior to the perfusion of the dye, in some experiments the surface of the brain was exposed immediately after the animal had been killed. Pressure of various degrees was then applied to the brain. In the subsequent supravital examination of the permeability of the brain vessels, small blue spots were visible both in the cortex and in the subcortical white matter of the traumatized area. In most of these blue spots blood cells that had passed through the vascular wall were not manifest outside the vessels, and, as was usually the case with the dye, followed the course of the vessel a short distance. In certain damaged vascular branches stasis had, however, occurred and prevented the perfusion of the dye solution.

It is thus obvious that the traumatic damage in these cases had caused a local vascular lesion. The continuity of the vessels was interrupted and their contents could escape into the surrounding tissues. (When corresponding experiments were performed on living animals the same kind of damage resulted except that the bleeding was more pronounced, ball hemorrhages often being a sign that the passage of the blood in these cases had taken place under a certain pressure.)

This goes to show that in the examination of the supravital permeability of the cerebral vessels great care is essential in the manipulation of the brain. This source of error is of less importance in animal experiments, because here no mechanical manipulation of the brain is necessary (the brain is perfused in situ). This is not, however, the case in the investigation of human brains, where it is necessary, for obvious reasons, to remove the brain before the perfusion of the dye.

(d) The Effect of Different Agonal Factors

In view of the fact that the experimental animals are generally killed in the quickest possible manner, it is conceivable that the results of animal experiments cannot be compared with corresponding examination results of human brains. Most people die after a period of agony during which different kinds of pathological conditions may develop in connection with e. g. inadequate circulation, insufficient

oxygenation of the blood, relatively high venous blood pressure, and a marked rise of the body temperature. In order to find out whether and to what extent these factors per se might lead to disorder in the permeability of the cerebral vessels a special series of experiments was performed. These experiments were made on animals under anesthesia (generally urethane in rabbits and dial in cats). Trpb. was injected intravenously in vivo, unless otherwise stated.

1. *Experiments with anoxia*

Anoxia combined with retarded or temporary cessation of the circulation was produced in a series of experiments on cats. The basiliary artery was clamped by means of a silver clip and the soft tissues of the neck were ligated, except the two carotid arteries and the two external jugular veins. Afterwards the two carotid arteries were clamped for varying intervals. An observation of the pial vessels showed that the blood stream was considerably retarded and sometimes altogether stopped. The circulation was obviously inadequate for the nutrition of the brain, the animals reacting with decerebrate rigidity (cf. *Pollock & Davis 1923*), sometimes with a transient apnea. When the carotid was again opened trpb. was given intravenously, and after the dye had had enough time to take effect, the animals were killed and their cranial vessels washed out in the ordinary manner with a saline solution and fixed with a formalin solution.

It might be added that in the positive cases in which the brain stained, the dye was confined substantially to the grey matter, in some cases staining almost the whole of the grey matter, in others, only patches and spots. In those cases in which the clamps were applied more than once, injections of trpb. solution were given between such applications and not only afterwards.

Results:

Exp. No.	Time clamped	Duration of subsequent circulation of dye	Macr. staining	Blood content of vessels	Fixation
1	5 min. $\times$ 10	1 hour	0	0	Good
2	15 " $\times$ 2	1 "	0	0	"
3	$\frac{1}{2}$ hour	4 "	0	0	"
4	1 "	2 "	0	0	"
5	1 "	1 "	(+)	+	Incomplete
6	1 "	5 "	+	+	"
7	1 + $\frac{1}{2}$ hour	1 "	(+)	+	"
8	1 + 1 "	1 "	+	+	"
9	7 hours	$\frac{1}{2}$ "	0	++	0

All the cases were examined microscopically. These inspections showed that the macroscopically conspicuous bluishness of the grey substance was due to the fact that the blood containing the dye-stuff had stagnated in the vessels. Those cases in which only patches were stained may be explained by the fact that in the unstained areas the vessels had been well rinsed, or contained unstained blood. In other words, the vessels were either open to the perfusion fluid and showed a normal permeability, or stasis had occurred before the injection of the dye, which was consequently unable to reach the vascular areas in question.

A close analysis of the contents of stained vessels showed that they did not always contain blood corpuscles, but often a bluish, cobweb-like reticle adhering to the vascular wall here and there only, whilst in other places a more homogeneous filling of coloured contents was observable. The whole picture was strongly reminiscent of coagulated, residual blood plasma.

In one case in which the clamps had been applied for a long time (7 hours) total stasis had arisen and completely obstructed the circulation and the entrance of the dye to the cerebral vessels.

This examination thus showed that local anoxia in the brain does not lead to a disturbance in the permeability of the cerebral vessels, even if the anoxia lasts over 1 hour (cf. results of dye perfusion after different post mortem intervals). After this interval, however, an increasing stasis and intravascular coagulation commences (possibly partially as a consequence of a gradual fall in the blood pressure and by the effect of the dye stuff) which renders impossible continued observation of the permeability of the cerebral vessels. This stasis is most pronounced in the grey matter.

It should be noted that in the supravital examination of human brains a macroscopic staining of the cortex and the basal ganglia was always manifest, and microscopic control showed that this staining was to be attributed to the fact that certain vascular branches were more or less filled with coloured contents (*Broman* 1944, 1947). This phenomenon is probably identical with that shown by the animal experiments described in this paper, and is presumably due mainly to agonal and post mortem stasis, and intravascular coagulation. A close study and comparison with conditions in supravitaly stained human brains also showed that the vessels and the vascular contents are microscopically similar in appearance to that in these experiments. Thus it is not a question of a disorder in the cerebral vascular permeability in this case, but of a stagnation of dye stuff adherent to intravascular clotted blood plasma.

2. *Experiments with increased venous pressure*

In three experiments on rabbits the large neck vessels (aa. carotis and vv. jugularis ext.) and trachea were laid bare and a snare placed around the rest of the neck and drawn tight at the same time as the jugular veins were repeatedly clamped for a few minutes. The result was that in all cases a few single, small blue-stained hemorrhages in the pons were produced.¹ For purposes of comparison a few more experiments were performed in which the animal was strangled, all the soft parts of the neck being clamped (also the carotid arteries and the trachea). In one of these experiments a small hemorrhage in the pons was discernible. A registration of the pressure in the cranial part of the jugular vein showed that also in this case a substantial increase in the pressure was present in the cranial veins (17 cm H₂O in the jugular vein) in spite of the clamping of the carotid arteries.

During this artificially produced stasis it was observed that the outer soft parts of the head had swelled (= a distinct edema), and when the skull was trephined and the surface of the brain exposed, there occurred a simultaneous herniation of the brain with the typical local circulatory disturbances, comprising a passage of blood corpuscles and dye in and below the herniated region (*Broman*—not published).

Attempts to increase the cranial venous pressure were also made by clamping the superior vena cava of rabbits, whose thorax was opened under anesthesia, the breathing being maintained by artificial respiration. Four such experiments, however, gave negative results. Neither did any edema of the head tissue arise, nor was the recorded increase in the pressure of the jugular vein so pronounced as in those cases in which the snare had been placed around the neck. In rabbits there are evidently sufficient collateral connections with the inferior vena cava to compensate for the effect of the stoppage of the superior vena cava in rabbits.

In three experiments performed on rabbits the brain surface was exposed as much as possible (to avoid the closed-box effect) and the animals were allowed to hang with their heads down. Neither in these cases could any disturbance in the permeability of the cerebral vessels be detected except that following on the herniation, i.e. confined to the borders of the exposed part of the brain.

In three experiments on guinea-pigs the animals were centrifuged

¹ In two more experiments the spinal vessels were compressed by an *écraseur* and the fall of the blood pressure was compensated by injections of adrenalin, but the result was the same.

at a rate of 6-8 revolutions per second and with their heads outward about 1 metre from the centre of rotation. But here again no disorder in the cerebral permeability was manifest except the usual local herniation damage in those cases that had been trephined.

Summarizing, it is thus possible to conclude that, except under extreme circumstances, a general increase in the cranial venous pressure is unable to give rise to a disturbance of the cerebral vascular permeability. When in certain cases a positive result was obtained, the only effect was small punctate hemorrhages, predominantly in the brain stem.

3. *Experiments with an agonal and post mortem elevation of the temperature*

These experiments were performed on rabbits that had been warmed up in various manners. In two cases the rabbit lay 30-60 min. on a heated operation table, during which the dye was injected intravenously. In one of these two cases the maximum throat temperature measured was 43°C ., and in the other case the maximum brain temperature (measured in one hemisphere that was, of course, damaged) was 42°C . In the first case the result was negative and in the other, a more or less pronounced disorder in the cerebral vascular permeability of the superficial layer of the brain was observed in the form of stained patches about 1 mm deep. The localization of the disorder in the poles of the undamaged hemisphere and the cerebellum was ascribable to the position of the animal, the region damaged being nearest the heated surface (and presumably heated to a higher degree than that recorded by the thermometer).

As this heating method permitted only a local warming of the animal, the experimental conditions were changed, and in three experiments the animal was submerged completely in a water bath (breathing through a tracheal cannula) that was then heated from $40 \rightarrow 46^{\circ}\text{C}$. in the course of one hour. The body temperature measured in the throat increased from $37 \rightarrow 45^{\circ}\text{C}$. This heating process affected the animals severely, and one of them died as a consequence. The result of these experiments was a slight disturbance in the permeability with a patchy passage of the dye in some superficial regions of the brain, most conspicuous in the cerebellum. The damage was about 1 mm deep. The limitation of the damage to the surface is to be ascribed to the fact that the animal also in these experiments was heated from the outside.

In three other experiments the animals were warmed up after

death. In all of them the blood had first been washed away with a saline solution. It was then found that if the animal was allowed to lie in water for half an hour at a temperature of about 45° C., the permeability of all the pial vessels and of some of the larger vascular branches in the brain stem was impaired. If the animal was allowed to lie for one hour or longer, the subsequent post mortem perfusion of the dye was rendered difficult or impossible (presumably owing to the absorption of the saline solution by the brain, as was the case in experiments with delayed post mortem perfusion of the dye, but still quicker in those cases in which the animal was allowed to lie in the warm water).

(e) *Result of Supravital Staining of a Cerebrovascular Disorder Experimentally Produced in Vivo*

Above a report has been given of an experimental examination of those factors that may give rise to sources of error in the supravital examination of the permeability of the cerebral vessels. The next step is to find out the results of such experiments when carried out on animals in which a disorder of the permeability has been experimentally produced in vivo.

Results:

Exp. No.	Time post mort.	Staining of the damaged region	Blood content of vessels in the damaged region	Fixation of the damaged region
1	5 min.	+	—	good
2	5 "	+	—	"
3	5 "	+	—	"
4	5 "	+	—	"
5	10 "	+	—	"
6	10 "	+	(+)	"
7	10 "	+	—	"
8	10 "	+	—	"
9	15 "	+	—	"
10	15 "	+	+	"
11	15 "	+	+	rather good
12	20 "	+	(+)	good
13	25 "	+	+	rather good
14	½ hour	+	+	" "
15	½ "	+	+	" "
16	¾ "	+	+	" "
17	1 "	(+)	+	poor
18	1 "	(+)	+	"
19	2 hours	—	+	none
20	2 "	—	+	"

The experiments were performed on guinea pigs and the injurious agent selected was sheep hemolytic rabbit serum injected into the right carotid artery ad modum *Forssman-Skoog*. The subsequent damage is well-known from earlier investigations. Its symptoms are distinct, and it is never so great as to cause a total stasis of the vessels, which are always passable (in contradistinction to most other forms of toxic lesions).

Examinations were carried out on 20 guinea pigs. After the experimental production of the damage the animals were killed and allowed to lie for varying periods before they were perfused with dye-solution.

It might be added that the staining in the damaged regions in those cases that were allowed to lie 15 minutes or more, was more or less patchy and located mainly to the periphery of the damaged region whose central portion, however, exhibited a more or less pronounced stasis with vessels containing blood (not washed out), and bad fixation. It is thus evident that a post mortem blockage takes place in the vessels of the maximally damaged area and that the supravital examination of disturbances in the vascular permeability is rendered difficult and finally impossible by this blockage.

The cause of this post mortem blockage appearing earlier in a damaged area than in intact regions of the brain is probably a latent edema in the damaged area, so that only a slight additional absorption of water is necessary to cause a stoppage of the vessels by compression. The absorption of water is probably also livelier in the damaged region, partly, on account of the disorder in the vascular permeability (= easier passage) and partly, as a consequence of the tissue damage (= increased absorption capacity for water). An intravascular coagulation of the blood may possibly also be more rapid in areas with vascular damage.

SUMMARY

Experiments were performed on animals to analyse the methodical conditions precedent for a supravital examination of the permeability of the cerebral vessels. Various sources of error and disturbing factors that might adversely effect the results and their evaluation were analysed. The following statements are made.

1. The examination should be performed as soon as possible post mortem. A delay of 1 hour or more will permit the development of an increasing obstruction of the cerebral vessels by a close packing of blood corpuscles and intravascular coagulation of the blood. If this obstruction is prevented by a rinsing of the vessels with a

- saline solution immediately post mortem, or preferably by the injection of heparin immediately before the animal is killed, the examination may be carried out after considerable delay. No disturbance in the cerebral vascular permeability was demonstrable as a result of the post mortem change of the vascular walls, until more than 12 hours after death (possibly earlier in man, whose body temperature does not fall so quickly as that of small animals).
2. The dye solution must be properly washed out before the fixation of the brain by the perfusion of a formalin solution, otherwise the permeability of the vessels will be damaged by the formalin whilst concentrated dye solution still remains in the vessels, and consequently a passage of the dye will take place through the vascular walls out into the surrounding tissues just as if the vessels had been damaged before the perfusion of the dye (e. g. *intra vitam*).
 3. If the brain is subjected to traumatic injury post mortem, the vessels will rupture and the dye will escape into the surrounding tissues in the form of small blue points.
 4. If the brain is subjected to retarded circulation and anoxia before the animal is killed, it will have no effect on the result of these investigations, provided that the cerebral circulation is not obstructed as long as one hour or more. After this time, however, the blood corpuscles begin to become closely packed and intravascular coagulation commences and block the vessels (as in the case in which the animals are allowed to lie one hour or longer before the commencement of a post mortem perfusion—cf. point 1). The blood stagnated above all in the grey matter, which may therefore macroscopically look somewhat blue on account of the stained stagnated blood content inside the vessels and not on account of a disturbance of the vascular permeability. It is probable that these phenomena may occur in man during agony.
 5. A general increase in the cranial venous pressure has no adverse effect on the vascular permeability unless of an extreme degree, when isolated small, punctate hemorrhages occur, especially in the brain stem. In man the occurrence of such an extreme increase of the venous pressure during agony seems in most cases to be improbable.
 6. Elevated temperature, if extreme, can cause a disturbance in the permeability of the cerebral blood vessels (slight signs of damage at about 45° C.). It is not probable that such temperatures ever occur in man, and if so, but exceptionally.
 7. In an area with disturbed permeability of the cerebral vessels and local edema *in vivo* the post mortem blockage of the vessels deve-

lops quicker than in intact regions of the brain. This can render the perfusion of the dye difficult and thereby also the demonstration post mortem that a disturbance in the permeability was present in vivo.

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A FOLLOW-UP STUDY OF PATIENTS
DISCHARGED FROM RØNVIK MENTAL HOSPITAL
DURING THE PERIOD 1938-1941

(215 treated and 232 nontreated cases)

By

L. EITINGER

The purpose of this work is that of studying (1) the effect of convulsion therapy in patients treated by this method in this hospital, and (2) the fate of the patients so treated after their being discharged from the hospital. In order to compare facts those discharged patients who have not undergone treatment are also included.

As an introduction some "historical" remarks may be justified. Convulsion therapy has been practised at Rønvik Hospital since March 1938. However, early in 1942 all patients from the hospital had to be removed to other hospitals owing to the hospital being requisitioned by the Nazis. The material is, therefore, limited to the four-year period 1938-1941. The observation period for the discharged patients thus varies from seven to ten years.

During the entire period use has been made of cardiazol—later on pentrozol—convulsion treatment as described by Meduna. Insulin treatment as described by Sackel has been used in two instances only, and has not, therefore, been considered in this material. Electro-shock treatment was first adopted after the period mentioned.

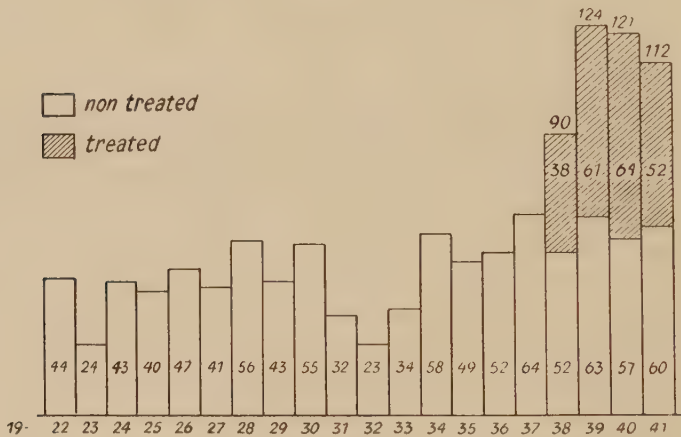
No serious complications have occurred during this four-year period. The commonest "complication" if it may be so called, has been dislocation of the jaw, which in all cases was reduced while the patient was still unconscious. Compression fracture of vertebrae occurred in fourteen cases and gave rise to a slight backache for several weeks—in one instance for a couple of months—but in no instance complications occurred which can be said to have produced permanent injury.

The first part of this work is not concerned with the diagnosis, but only with obtaining a numerical expression of the part played by the convulsion therapy as to the capacity of the hospital.

I.

The essential feature is that the circulation of patients increased. In order to elucidate this statistically the number of patients discharged during the last twenty years of normal conditions at the hospital have been recorded as shown in Table 1. Patients who died in the hospital are not included.

TABLE 1
Patients Discharged During the Period 1922-1941.



The table shows that comparatively few patients were discharged each year. During the years 1922-1937 the number varies from about 25 to 60 patients per year. In 1938 the number increased to 90 and has, during the following years, varied from 110 to 120. As mentioned, the use of convulsion therapy was adopted at Rønvik Hospital in 1938. Further, it will be seen that the number of patients discharged without receiving treatment also during the years 1938-1941 remains at the same level as during the previous years. The number of cases treated comes in addition to the number of those not treated and thus contributes to an increase of the hospital capacity of about 100 per cent.

An objection to the table may be that a contingent increase in number of beds has contributed to the increased capacity. In order to eliminate this possible source of error a graph has been made (Fig. 1) showing not the actual number of patients discharged, but the

percentage discharge of the average number of beds occupied during the various years (Fig. 1). The annual discharge is thus about 15 per cent. up to 1939 when the curve suddenly rises above 30 per cent. simultaneously with the adoption of the convulsion therapy. The dotted curve, which represents the percentage discharge of nontreated patients remains at the same level as during the previous years when convulsion therapy was not practised. The graph thus shows the same as Table 1.



Fig. 1.

In the literature it is generally recognized that the course of the disease can be shortened by convulsion therapy. The author has tried to elucidate this in a table showing the average hospitalization period for patients discharged from Rønvik Hospital (Table 2).

TABLE 2
Average Hospitalization Period per Patient.

1928/29/30/31	1938/39/40/41		
Prior to convulsion therapy	Nontreated	Treated	All patients
1478 days	839 days	273 days	563 days

The first column represents the average hospitalization period (in days) during the period 1928-29-30-31 i.e. about 10 years prior to the adoption of the convulsion therapy. This was about 20 years ago when neither systematical occupational therapy nor home nursing existed. These figures are therefore only intended for a historical comparison as a contrast to modern therapy.

The table shows that the average hospitalization period during the years 1928-29-30-31 was 1478 days per discharged patient, i.e. about four years. During the four-year period 1938-1941, i.e. ten years later, the average hospitalization period had fallen to 563 days for all discharged patients. But a further analysis of this figure as to the ratio between treated and nontreated cases discharged during these four

years shows that the average hospitalization period for the nontreated was 839 days, i.e. fully two years, whereas the average hospitalization period for cases treated was 273 days, i.e. less than one year.

The next step is to find out in what condition the various patients were discharged during this four-period. This means the result of the hospitalization as regards the various patients, i.e. those having as well as those not having undergone convulsion therapy. The result is shown in Table 3.

TABLE 3
Patients Discharged 1938/39/40/41.

Treated				Nontreated				Total number discharged 1938/41
Not mental	Mental, improved	Mental, not improved	Total	Not mental	Mental, improved	Mental, not improved	Total	
87	116	12	215	74	76	82	232	447
40.4 %	54 %	5.6 %	100 %	31.8 %	32.8 %	35.3 %	100 %	
203				150				
94.4 %				64.7 %				

As will be seen in the table the patients discharged were classified as (1) "not mental", (2) „still mental, but improved", and (3) "mental, not improved".

The patients classified as "not mental" are those who on leaving the hospital are fully capable of work and who do not display signs of an active psychosis and where it is not justified to declare the patient insane. Patients discharged as "still mental but improved" may also resume their usual work, but certain circumstances may necessitate that the declaration of insanity is maintained. The disease may be of such a character that a relapse is likely to occur, or social circumstances, e.g. matrimonial problems, may not justify declaring the case as cured. Patients discharged as "mental, not improved", are those affected with chronic psychosis, having entered such a state that nursing outside hospital is possible. Owing to the great shortage of mental hospital beds in this part of the country (Northern Norway) the latter method of attendance has been practised as far as possible. As will be evident from what is just said above, it may be a matter of opinion whether a patient should be discharged as "not mental" or "still mental, but improved". This possible source of error is insignificant as regards this study because the same classification has been used regarding treated as well as

nontreated cases. More stress has perhaps been laid upon not declaring the case "not mental" owing to our being a little suspicious as to the duration of the remissions during the early years of convulsion therapy. At least this circumstance does not influence the results in a positive direction regarding the result of the convulsion therapy. However, in order to avoid this possible source of error in the after-examination, the patients discharged as "not mental" or "still mental, but improved" have been considered as one large group termed "socially recovered".

Table 3 shows that of the cases treated 5.6 per cent. only were discharged as "mental, not improved", whereas this term had to be applied to 35.3 per cent. of the cases not treated. The distribution is otherwise shown in Table 3.

II.

Stimulated by these rather encouraging figures we have followed up all the patients discharged in order to determine the duration of the remissions and as a whole obtain an impression of the further fate of the individual.

The after-examination was carried out in 1947 for patients discharged during the period 1938-1940, and in 1948 for patients discharged during 1941. The observation period thus varies from seven to ten years. The task of carrying out such an after-examination in Northern Norway was rather difficult. Almost one third of the district covered by Rønvik Hospital was totally damaged during the war, and the whole population was evacuated to southern parts of Norway. The medical administration was innovated during as well as after the war, a fact which resulted in the doctors being overloaded with other work so that they could not often spare the time for answering our questionnaires. However, despite these drawbacks we got a 88.5 per cent. response to our inquiries.

The follow-up study has been carried out as follows: (1) We made direct inquiries to (and received answers from) all Norwegian mental hospitals as to whether any of the patients discharged from Rønvik Hospital during the period mentioned had been admitted to one of them. (2) We wrote to the local medical officers at the home town or village of the patients and asked them to make inquiries about the patient's condition. (3) Finally we wrote directly to the patient's relatives. The questions to the medical officers and the relatives of the various patients aimed at having it ascertained whether the patient was healthy and carrying out work as before the onset of the disease, whether he had any psychic defects and if so, of what kind, or

whether he had been admitted to other hospitals or given rise to serious nursing problems.

The questionnaires to the patient's relatives were somewhat simpler.

Naturally we received the more extensive information about patients who had been readmitted and/or taken care of in private institutions, whereas recovered patients had often left their home town or village and sometimes could not be traced. We think, therefore, that poorer results would scarcely have been obtained if these missing cases had been included in the statistics also. The results of the after-examination are summarized in Table 4, the patients being divided into six different groups.

TABLE 4
Patients Discharged 1938/39/40/41.

Patient's present condition	Treated				Nontreated				Total
	Not mental	Mental, improved	Mental, not improved	Total	Not mental	Mental, improved	Mental, not improved	Total	
Completely socially recovered	57	61	2	120	39	24	4	67	187
Soc. recovered with psychic defects	3	11	—	14	12	14	—	26	40
Died from intercurrent diseases, not mental	3	2	—	5	3	8	—	11	16
Soc. recovered after repeated hospitalization	7	12	—	19	10	4	—	14	33
Nursing required or readmitted to hospital	3	15	8	26	5	5	53	63	97
Died in private institutions or mental hospitals	—	2	2	4	—	8	18	26	30
Total	73	103	12	188	69	63	75	207	403
Not answered	14	13	—	27	5	13	7	25	44
Total	87	116	12	215	74	76	82	232	447

(1) *Completely socially recovered* indicates not merely the patient's ability to carry out his usual work, but that on the whole he behaves as he did before the onset of the disease (Braatøy's "recovered").

(2) *Socially recovered with psychic defects* indicates patients who are able to resume their usual work, but who are rather odd at times, or may have occasional fits of depressions, etc. (Braatøy's "improved").

Such a grouping may easily involve the errors of a subjective evaluation. But this is no doubt insignificant in this work. The evaluation and the grouping into various "present conditions" have largely been done by the district medical officers who did not know whether the patient had received convulsion treatment or not. In other instances, too, i.e. where information was obtained from the family, the evaluation of the patient's present condition was given *before* it had been established whether the patient had received treatment or not.

(3) Group 3 includes patients who died in their homes from intercurrent diseases—otherwise psychically normal patients—as this group cannot be combined with the group including patients who died in mental hospitals from or during the course of a mental disease.

(4) This group includes patients who after the discharge from Ronvik Hospital have been readmitted but are socially recovered following a transient relapse.

The last two groups, (5) nursing cases or readmitted hospital cases, and (6) cases having died in an asylum or in private institutions, need no further explanation.

Group 5 is rather extensive and is in the literature usually subdivided into "home nursing cases" and "hospital cases". In this material such a subdivision does not seem justified owing to the fact that rather a great number of patients who were actually in need of hospital care had to be attended in their homes or in private institutions owing to the shortage of hospital accommodation. A subdivision has, therefore, been omitted, as it would not give a true impression of the patient's present condition.

The group of patients discharged as "mental, not improved" is insignificant as regards the *duration of the effect of the treatment*, because in this group the vast majority represents nontreated cases who as mentioned are chronic ones where the condition during the course of a prolonged hospitalization has entered such a pacified stage that the patient may be nursed in a private home. If these patients were to be included in the control material a correct picture would not be obtained, among other things because of the long hospitalization period needed for these patients. This group has therefore, been disregarded in the further discussion.

It may be mentioned, however, that six remissions occurred in this group (2 treated and 4 nontreated) showing that spontaneous remission may occasionally occur even in very long standing cases.

In order to give a better-arranged presentation of the results of the after-examination, the categories "not mental" and "still mental, but improved" have been merged in one group as "socially recovered".

The results of the after-examination thus surveyed is shown in Table 5.

TABLE 5
Present Condition of Patients Discharged as "Socially Recovered".

Present condition	Treated		Nontreated	
	Number	%	Number	%
Completely socially recovered	118	58.12	63	42
Socially recovered with psychic defects	14	6.9	26	17.33
Died from intercurrent diseases —not mental	5	2.46	11	7.34
Socially recovered after repeated hospitalization	19	9.36	14	9.33
Nursing required, or readmitted to hospital	18	8.87	10	6.66
Died in private institutions or mental hospitals	2	0.99	8	5.34
Not answered	27	13.3	18	12
Total	203	100	150	100

The main feature is that the incidence of "pure remissions", i.e. complete social recovery, is considerably higher in treated than in nontreated cases. The difference is fully 16 per cent., i.e. a little larger than the difference found by *Hinko & Lipschutz* (7) regarding remissions in treated and nontreated patients. The incidence of "socially recovered with psychic defects" is higher in nontreated than in treated cases (approx. 10 per cent.).—As to the remaining groups there is no essential difference except for the number of patients who died (recovered as well as nonrecovered cases) which is larger for the nontreated patients, a circumstance which most likely is due to the fact that the elderly patients did not receive convulsion treatment. If the groups "nursing cases hospital cases, and died in hospital or private institutions" are considered as a whole under the term "permanent relapse" it will be seen that there is a slightly higher incidence rate among the nontreated cases (12 per cent. as against 9.8 per cent.).

Statistical calculation shows that the difference between treated and nontreated is reliable.

P (the probability of incidental circumstances) is less than 0.01.

These improved results regarding patients having received convulsion therapy, particularly the group of "pure remissions" necessitated a further investigation of the diagnosis. The aim is then to determine which patients have undergone treatment and which have not, and

whether there is a higher tendency to spontaneous remissions in treated patients than in nontreated patients, i.e. whether the result of the treatment can be regarded as "post and non propter".

Most reports regarding following up of the result of treatment do not include an adequate control material, and even when nontreated cases are included these originate from different periods or from different hospitals, and *Faurby's* (6) postulation that "the author must present a control material which is from the same hospital and which shows the incidence of spontaneous remissions" consequently will scarcely be fulfilled. Faurby asserts this on the basis of "the varying conception of schizophrenia". Even if Braatøy (2) has shown that this "varying conception" actually does not vary to any great extent at Norwegian mental hospitals, it is always an advantage as regards the evaluation that the material is as homogeneous as possible, particularly if not merely conditions regarding a single disease are to be investigated.

The author thinks the postulate regarding a homogeneous material and control material is fulfilled here as far as possible for the following reasons:

- (1) During the entire four-year period (except for a period of a few months) the same chief physician has been in charge of Rønvik Hospital.
- (2) The diagnoses are "revised diagnoses" at the time of the discharge of the patients.
- (3) When a patient leaves the hospital —practically without exception—the diagnosis is always assigned by the chief physician, and it is also he who in the individual case decides whether the patient is to be discharged as "not mental", "still mental, but improved", or "mental, not improved". During the absence of the chief physician all the case journals are placed on his desk, and only in the most obvious cases will his substitute assign the diagnosis and the discharge category.

The (hypothetical) source of error which may be involved by a contingent disagreement as concerns the diagnosis, must under these circumstances be regarded as insignificant and can safely be disregarded in this material which concerns a comparison of two uniformly confined groups.

All patients who could not be contacted have been excluded, and in the remaining cases discharged from the hospital the diagnoses are shown in the following two tables.

TABLE 6
Discharge Diagnoses (Questionnaire Answered).

Diagnosis	Treated		Nontreated	
	Number	%	Number	%
	188	100	207	100
1. Schizophrenia	131	69.8	83	40.9
1a. Schizophrenia?	7	3.7	—	—
2. Psych. e constitutione	23	12.2	34	16.4
3. " manico-melancolica	18	9.6	20	9.7
4. " symptomata	1	0.5	11	5.3
5. " ex imbecillitate	1	0.5	9	4.4
6. " epileptica	—	—	9	4.4
7. " alcoholica	—	—	2	1.0
8. " ex involutione	2	1.1	11	5.3
9. " syphilogenes	—	—	10	4.8
10. " aliae vel mal. def.	2	1.1	1	0.5
11. Neurosis	3	1.5	12	5.8
12. Non insania (observ.)	—	—	5	2.4
Total	188	100	207	100

TABLE 6 a
Discharge Diagnoses for "Socially Recovered" Patients
(Questionnaire answered).

Diagnosis	Treated			Nontreated		
	Num- ber	%	Percen- tage of total number dis- charged	Num- ber	%	Percen- tage of total number dis- charged
	176	100	93.6	132	100	63.8
1. Schizophrenia	120	68.2	91.6	36	27.3	43.4
1a. Schizophrenia?	7	4.0	100	—	—	—
2. Psych. e constitutione	22	12.5	95.6	27	20.5	79.4
3. " manico-melancholica	18	10.2	100	18	13.6	90.0
4. " symptomata	1	0.6	100	10	7.5	90.9
5. " ex imbecillitate	1	0.6	100	2	1.5	22.2
6. " epileptica	—	—	—	5	3.8	55.5
7. " alcoholica	—	—	—	1	0.8	50.0
8. " ex involutione	2	1.1	100	7	5.3	63.6
9. " syphilogenes	—	—	—	8	6.0	80.0
10. " aliae vel mal. def.	2	1.1	100	1	0.8	100
11. Neurosis	3	1.7	100	12	9.1	100
12. Non insania (observ.)	—	—	—	5	3.8	100
Total	176	100	93.6	132	100	63.8

Table 6 *a* shows the absolute number as well as the percentage of patients discharged as "socially recovered" according to the various diagnoses (all questionnaires answered).

The table shows that the vast majority of patients who have received treatment (95 per cent.) belongs to the following groups: schizophrenia, psychosis *e* constitutione, and psychosis manico-melancholica. The remaining groups are only sparsely represented. "Schizophrenia?" has been confined as a special group. This may need a little further explanation. On admission these patients represented a clinical picture which in all respects resembled a schizophrenia, but the rapid improvement in conjunction with the treatment did not fully justify the diagnosis. But neither was another diagnosis justifiable, so we preferably used the term "schizophrenia?".

The case of psychosis *symptomatica* who was treated was actually a case of presenile melancholiform psychosis, but the climacteric changes were here so marked that "psychosis *symptomatica*" was no doubt the correct classification. (The patient has now recovered completely).

The case of psychosis *ex imbecillitate* which was treated was a boy whose complaint had originally been diagnosed "schizophrenia in an imbecile", but when the patient was discharged the diagnosis was changed to psychosis *ex imbecillitate*. He was discharged under the category "still mental, but improved" and has resumed useful employment and lives at home under normal conditions. The case must, therefore, be regarded as socially recovered. Both patients who were treated for "psychosis *ex involutione et senio*" showed melancholiform conditions which occurred in the (pre)senium and where the diagnosis psychosis manico-melancholica owing to the sparse clinical symptoms was not justifiable. It should be mentioned, however, that these cases of melancholiform conditions in the fifth and sixth decades have, particularly during recent years, been an increasing occurrence. A more accurate diagnostic classification of these conditions (psychosis *symptomatica*, psychosis manico-melancholica—contingently psychosis *e* constitutione—psychosis *ex involutione et senio*) is rather difficult and is often a matter of opinion according to which symptom is the predominant one.

The fifteen cases of neurosis (3 treated, 12 nontreated) in the table include psychogenic depression, war neurosis (April 1940), neurasthenia, sexual neurosis, etc. The number of cases being so small, only three cases having received treatment, is primarily due to the fact that during the four-year period we had no special ward for neuroses (voluntary hospitalization). In these cases we preferred to omit treat-

ment, particularly owing to the subjective discomfort involved by the pentozol treatment.

Later on, however, conditions changed. Almost 30 per cent. of our patients are now admitted at their own wish, and we have used electroshock more widely in cases of neurosis where all other attempts at treatment (sedativa, and perhaps the rather more occasional unorganized psychotherapy which can be practised by the few physicians in charge of so many patients) have failed.

However, on the whole it can be said that the groups 5-13 are insignificant with a view to follow-up and control material. In the following part of this work these groups have been disregarded. We have, therefore, chosen to concentrate upon the groups 1-3 and upon patients discharged as "socially recovered".

Consequently, the problems which arise are the following:

What is the present condition of these patients? Is the remission as caused by the treatment of shorter or longer duration than the spontaneous remissions? Is the increased hospital capacity as shown here real or just imaginary?

1. SCHIZOPHRENIA

The result of the following-up of these patients is shown in the following table:

TABLE 7
Schizophrenia.
Patients Discharged as "Socially Recovered".

Present condition	Treated			Nontreated		
	120 + 7			36		
	Number	%	Average hospitalization period in days	Number	%	Average hospitalization period in days
Completely socially recovered	79+7	65.8	100+95	19	52.8	420
Soc. recovered with psychic defects	8	6.7	213	9	25.0	579
Died from intercurrent diseases, not mental	2	1.7	81	2	2.5	437
Soc. recovered after repeated hospitalization	14	11.6	238	1	2.8	685
Permanent relapse	17	14.2	777	5	13.9	978
Total	120+7	100	264	36	100	617

The striking feature here is the high incidence of remissions. The literature contains no adequate material for comparison, as most after-examinations include all patients discharged, whereas we have included only those patients who have been discharged as "socially recovered". Our aim was primarily to investigate and compare the duration of remissions in treated and nontreated patients. Consequently we think—as previously mentioned—that the correct thing to do is to exclude all patients who have been discharged as not improved and as nursing cases.

Further, the table shows that the incidence of permanent "pure remissions" is 13 per cent. higher in treated than in nontreated cases, and that the incidence of "recovery with psychic defects" in nontreated cases is four times that of treated cases. Further, it will be seen that the number of deaths is larger in nontreated cases, whereas "permanent relapse" is about equally frequent in both groups. On the other hand, there are four times as many transient relapses in treated as in nontreated cases. However, most important to us is the fact that the average hospitalization period (in days) per patient for nontreated cases is more than twice that for treated cases. The table will be more closely discussed in a later paragraph.

Statistical calculation shows that the difference between treated and nontreated cases is reliable.

P (the probability of incidental circumstances) is less than 0.01.

The result of this survey is, to a certain extent, in favour of the treated cases, and the problem naturally arises as to the severity of the various cases.

When we first started convulsion therapy at Rønvik Hospital we had no definite indications for this treatment in schizophrenia. Nor, unfortunately, was every second patient treated as suggested by Scharf-fenberg (15) in order to obtain an adequate control material. In the beginning treatment was preferably given to patients from whom we had the impression that there was little to lose and much to win—to quote *Braatoy* (3)—i.e. to particularly difficult patients with the presumably worst prognosis. Successively the treatment was more widely used, but the tendency to use expectant and conservative treatment has always been greater for apparently milder cases than for serious ones. However, this is only an impression obtained from statements given by the physicians who were employed at the hospital during the period 1939-1941. By studying the journals it has not been possible to find accurate reasons as to why some patients received

treatment while others did not. However, in order to get a criterion for the severity of the disease and thus the effect of the treatment, the material has been studied with a view to the following:

- (a) Heredity.
- (b) Information concerning the first or recurrent phases of the disease.
- (c) The duration of symptoms on admission.
- (d) Age at the onset of the disease.

We are fully aware of the fact that these four factors alone do not determine the course of the disease, spontaneous remissions, etc. However, to include all factors pointed out by Langfeldt (9) which affect the course of the disease, is impossible owing to the way in which the after-examinations were carried out. The journals do not, for instance, convey sufficient information as to body build, premorbid personality, etc., for statistical conclusions. For the same reason a grouping into various schizophrenic types (katatonic type, hebephrenia, paranoid forms, etc.) or typical or atypical forms (Langfeldt) has not been attempted. If such a grouping should be applied to all patients discharged it would necessitate all cases diagnosed as schizophrenia being revised. The intention of this work would be futile if a statistical presentation of material was given which had not been diagnosed and evaluated by the same person, without a view to comparison or any kind of revision whatsoever. Different subjective views would be involved, views which might possibly be influenced by the course of the disease after the discharge from the hospital. In order to eliminate this possible source of error a grouping as mentioned has been avoided as far as possible. Moreover, the material includes all patients discharged over a comparatively long period so that most of the groups mentioned are equally represented in treated and in nontreated cases.

The sex of the patients has also been disregarded. Even if it is sometimes stated in the literature that females usually respond to treatment better than males, Dedichen (5) and Christiansen (4) et al. have shown that the difference is not sufficiently marked to exclude its being incidental. The difference is about the same in treated as in nontreated cases. For these reasons, and because of the comparatively small number of cases much of the general survey would be lost by further subdivision. A classification according to the sex has therefore been omitted.

(a) *Heredity.*

The data concerning familial occurrence are based upon the information given by the doctor referring the patient to the hospital, and the information volunteered by the patients during his stay in the hospital. All cases in which hereditary predisposition might have been present probably are not included, but this source of error is insignificant for the result as a whole, as it can be assumed that it is equally represented in treated and nontreated cases (Table 8). Consideration has not been given to the question whether one or several cases of mental disease have occurred in the family.

In the table “+” indicates familial predisposition while “—” indicates absence of such predisposition. “+” thus indicates the presence of mental disease in parents, grandparents, offspring, and siblings. Addiction to drink, and suicide in the absence of mental disease, odd behaviour, etc., in the family have not been regarded as hereditary factors. The result is shown in Table 8.

TABLE 8
Heredity.

Present condition	Treated			Nontreated		
	+	—	Total	+	—	Total
Compl. soc. recovered	37+3	42+4	79+7	9	10	19
Soc. recovered with psychic defects	4	4	8	4	5	9
Died from intercurr. diseases, not mental	—	2	2	2	—	2
Recovered after re- peated hospitalization	6	8	14	—	1	1
Permanent relapse	5	12	17	2	3	5
Total	52+3 43.3 %	68+4 56.7 %	120+7	17 47.3 %	19 52.7 %	36

This material is not conclusive as to the effect of heredity on the prognosis even if there is a slight “—” preponderance regarding permanent relapse. We could not, however, confirm, as stated in the literature, that the prognosis is better for cases with familial predisposition than for those without (Langfeldt (9)). *Determinative of our investigation, however, is only the fact that heredity is about equally represented in treated and in nontreated cases.*

The result is statistically reliable as $P = 0.08-0.09$.

(b) *Initial or recurrent phases of the disease.*

Based upon the assumption that a recidivation process, i.e. a recurrent phase of the disease, is apt to have a worse prognosis or shorter remission than the initial phase, the material has been investigated with this in view. The result is shown in Table 9.

TABLE 9
Initial of Recurrent Phase of the Disease.

Present condition	Treated			Nontreated		
	Initial phase	Recurrent phase	Total	Initial phase	Recurrent phase	Total
Compl. soc. recovered	68+7	11	79+7	17	2	19
Soc. recovered with psychic defects	6	2	8	5	4	9
Died from intercurr. diseases, not mental	1	1	2	—	2	2
Recovered after re- peated hospitalization	8	6	14	1	—	1
Permanent relapse	9	8	17	3	2	5
Total	92	28	120+7	26	10	36
	76.7 %	23.3 %		72.2 %	27.8 %	

The table shows that the incidence of "permanent pure remission" is highest in the initial phase of the disease in treated as well as in nontreated cases, whereas "permanent relapse" is about equally represented in the initial as well as the recurrent phases of the disease. *For our investigation, however, the only fact of importance is that the distribution of "initial phase" and "recurrent phases" is practically the same in treated and in nontreated cases.*

Statistical calculation shows that P is 0.09.

(c) *Duration of symptoms on admission.*

Most authors (Kalinowsky and Hoch (8), Sargant and Slater (14), Dedichen (5), et al.) agree that the duration of symptoms before treatment is instituted is of great importance to the prognosis. Langfeldt (10, 11) points out an essential difference between typical and atypical types of schizophrenia and shows that it is of no consequence whether the typical schizophrenias are treated early or late in their course, which is inevitably progressive. The prognosis of atypical forms, however, is better the shorter the duration of the disease when treatment is instituted. In this comparative survey, however, where no

differentiation has been made as to the various types, the duration of symptoms before admission should no doubt be considered. In the literature there is no agreement as to how long a case can or should be regarded as "acute", or when it is to be classified as "chronic", and the duration of acuteness is stated to vary from a couple of months to years in the various statistics. Here it has been decided to divide the patients into three groups, viz. one group with a duration of symptoms up to three months—which is no doubt to be regarded as a minimum, particularly with a view to the long travelling distances in Northern Norway where the very transport of the patient to the hospital often takes more than a week; the mails (admission papers, etc.) take just as long—a second group with a duration of symptoms from three to twelve months, and a third group representing "chronic" cases with a duration of symptoms of more than a year. The result is shown in Table 10.

TABLE 10
Duration of Symptoms on Admission.

Present condition	Treated				Nontreated			
	I	II	III	Total	I	II	III	Total
Compl. soc. recovered	43+7	24	12	79+7	12	5	2	19
Soc. recovered with psychic defects	3	2	3	8	2	—	7	9
Died from inter-current diseases, not mental	—	2	—	2	—	—	2	2
Recovered after repeated hospitalization	5	5	4	14	—	—	1	1
Permanent relapse	2	4	11	17	2	2	1	5
Total	53	37	30	120+7	16	7	13	36
	44.2 %	30.8 %	25.0 %	100 %	44.4 %	19.4 %	36.2 %	100 %

I Duration up to 3 months

II Duration from 3 to 12 months

III Duration more than one year

Even if this subdivision results in the figures obtained being too small for definite conclusions, it is evident that there is a definite preponderance of remissions in cases of short standing, and, parti-

cularly in treated cases, a preponderance of chronic cases in the group "permanent relapse". The fact is striking also in that 7 out of 9 nontreated patients classified as "recovered with psychic defects" have a duration of the disease of more than one year, whereas the treated patients show a more even distribution. However, the figures are so small that incidental circumstances cannot be disregarded.

A comparison between treated and nontreated cases shows that the incidence in group I, i.e. patients with a duration of symptoms of up to three months, is the same. Even if there are some small differences in the groups II and III, these are probably insignificant as to the postmorbidity course. *Hence, it seems justified to assume, that the material as concerns the duration of the disease prior to the admission shows no essential difference in treated and nontreated cases.*

Statistical calculation for the group II and III as a whole shows a P of 0.01.

(d) *Age at the onset of the disease.*

The problem whether the age of the patient at the onset of the disease is of any consequence to the prognosis has been widely discussed in the literature. Even if the results are not as synonymous as those published by Mauz (13), it is almost generally recognized that the prognosis is worse in younger individuals, particularly in those below the age of 25 (Langfeldt, 23 years).

The distribution according to age in our material is shown in Table 11.

Even if the figures also here are too small to allow of definite conclusions, they largely correspond to those appearing in the literature. In the group of "completely socially recovered" fully one half of the patients were below the age of 25, whereas the other half is distributed among all the remaining groups. In the group of "permanent relapse" practically all the patients were below the age of 35.

A comparison of treated and nontreated cases shows that there is a preponderance of the younger age group as concerns treated patients, which might indicate a worse prognosis. The difference, however, is eliminated by the next group (25 to 35 years), so that *here also the distribution according to age is practically the same in treated and nontreated patients.*

Summarizing the results it may be said that the material as concerns the criteria mentioned shows no essential difference as to treated and nontreated cases, and a comparison with the figures as presented in Table 7 is, therefore, justifiable. The conclusion is that in patients having undergone convulsion therapy there is

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TABLE 11
Age at the Onset of the Disease.

Present condition	Treated						Nontreated					
	-25	-35	-45	55	over 55	Total	-25	-35	-45	-55	over 55	Total
Compl. soc. recovered	41	27	9	2	—	79	11	5	—	2	1	19
Soc. recovered	6	2	—	—	—	8	4	4	1	—	—	9
with psychic defects	—	1	1	—	—	2	—	1	1	—	—	2
Died from intercurrent diseases, not mental	9	4	—	1	—	14	—	1	—	—	—	1
Recovered after repeated hospitalization	13	3	1	—	—	17	2	3	—	—	—	5
Permanent relapse	69	37	11	3	—	120	17	14	2	2	1	36
Total	57.5 %	30.8 %	9.2 %	2.5 %	—	100 %	47.2 %	38.8 %	5.6 %	5.6 %	2.8 %	100 %

- (1) *probably* a higher incidence of pure remissions,
- (2) *probably* a lower incidence of imperfect recovery,
- (3) *a considerable and definite* shortening of the course of the disease.

This investigation also seems to settle Langfeldt's (11) question that "perhaps this shortening of the disease does not represent an advantage, as the spontaneous remissions—possibly as a result of biológico-humeral changes which serve to prevent recidivation—in the long run serve the patient best" as it appears that the spontaneous recovery in no way differs from the recovery produced by convulsion therapy in patients discharged from this hospital.

2. PSYCHOSIS E CONSTITUTIONE

The other group of patients which has been investigated comprises patients discharged with the diagnosis "psychosis e constitutione". For reasons previously stated a definition or a discussion as concerns the diagnosis in these cases will not be attempted (Braatøy (2)). A total of 23 treated and 34 nontreated cases have been discharged with this diagnosis. 22 (95.6 per cent.) of the treated cases and 27 (79.4 per cent.) of the nontreated were discharged as "socially recovered".

The present condition of the patients is shown in Table 12.

TABLE 12
Psychosis e Constitutione.
Patients Discharged as "Socially Recovered".

Present condition	Treated		Nontreated	
	22		27	
	Number	Average hospitalization period in days	Number	Average hospitalization period in days
Completely socially recovered	15	159	10	501
Soc. recovered with psychic defects	3	127	10	361
Died from intercurrent diseases, not mental	2	672	1	1020
Recovered after repeated hospitalization	1	82	4	394
Permanent relapse	1	111	2	228
Total	22	230	27	501

Despite a different diagnosis the results are largely the same as for the patients suffering from schizophrenia. However, there is a slightly

higher incidence of permanent pure remissions in the treated cases and also a higher incidence of imperfect recovery in the nontreated cases. The average hospitalization period per patient is considerably shorter here also for treated than for nontreated cases.

The diagnostic group of "psychosis a constitutione" has not been paid the same great attention in the literature as schizophrenia, and it seem difficult, therefore, to ascertain whether the criteria chosen are of major importance as concerns the duration of the remissions and the fate of the patients otherwise. The figures do, however, give a certain indication as to the composition of the material. Owing to the small number of cases a grouping into different "present conditions" has not been attempted and the result is presented as a whole for all four categories.

For the same reason a calculation of incidence rates as well as detailed statistical calculations has been omitted.

TABLE 13
Psychosis e Constitutione.

	Treated				Nontreated			
	Familial occur.		No fam. oc.		Familial occur.		No fam. oc.	
Heredity	7		15		6		21	
	Initial		Recurrent		Initial		Recurrent	
Initial or recurrent phase	15		7		18		9	
	I		II		I		II	
Duration of symptoms on admission	8		9		6		10	
	I		II		I		II	
Duration of symptoms on admission	8		9		6		10	
	I		II		I		II	
Duration of symptoms on admission	8		9		6		10	
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Duration of symptoms on admission	8		9		6		10	
	I		II		I		II	
Duration of symptoms on admission	8		9		6		10	
	I		II		I		II	
Duration of symptoms on admission	8		9		6		10	
	I		II		I		II	
Duration of symptoms on admission	8		9		6		10	
	I		II		I		II	
Duration of symptoms on admission								

Heredity has been recorded and evaluated as in schizophrenia and the *distribution according to heredity is about the same in both groups. The same applies to the question whether the patient was admitted for the first time or readmitted to the hospital.* Regarding the duration of the disease prior to admission there are some variations, so this has been considered in detail as shown in Table 14.

TABLE 14
Duration of Symptoms on Admission.

Present condition	Treated			Nontreated		
	I	II	III	I	II	III
Completely socially recovered	6	8	1	4	4	2
Socially recovered with psychic defects	1	1	1	1	4	5
Died from intercurrent diseases, not mental	1	—	1	—	—	1
Recovered after repeated hospitalization	—	—	1	1	2	1
Permanent relapse	—	—	1	—	—	2
Total	8	9	5	6	10	11

Here the groups I, II, and III also indicate the duration of symptoms prior to admission, three months, one year, and more than one year, respectively.

It will be seen that nontreated cases to a far higher degree have been admitted after suffering from their disease for more than a year, whereas two thirds of the treated cases display a duration of symptoms of less than one year. Whether this difference is a determining factor to the postmorbidity course can be ascertained only with difficulty on the basis of so few cases. However, it is pointed out that one half of the nontreated cases of imperfect recovery and all cases of "permanent relapse" belong to Group III, whereas the majority of the cases of pure remission belong to Group II. This applies to treated as well as nontreated cases.

Concerning the distribution according to age there are perhaps more patients above the age of 45 in the nontreated group, a fact which may indicate a more favourable prognosis in these patients, but the difference is scarcely great enough to be considered as a determining factor, and *on the whole there is little difference between the distributions in the two groups.*

With the previously mentioned reservations, *the patients discharged with the diagnosis psychosis e constitutione on the whole show an even distribution as to the two groups so that here also the conclusion is:*

- (a) *probably* higher incidence of permanent pure remissions,
- (b) *probably* a lower incidence of imperfect recovery,
- (c) *a definite shortening of the course of the disease in treated patients.*

3. PSYCHOSIS MANICO-MELANCHOLICA

During the four-year period mentioned a total of 38 patients were discharged with the diagnosis of psychosis manico-melancholica. Of these 18 underwent convulsion therapy and were discharged as "socially recovered". Of 20 nontreated cases 2 were discharged as "mental, not improved" and 18 as "socially recovered". The present condition of the patients is shown in Table 15. Incidentally, the number of cases is the same on both sides. For this reason, but also owing to the low figures, a calculation of incidence rates and detailed statistical calculations have been disregarded.

TABLE 15
Psychosis Manico-Melancholica

Present condition	Treated		Nontreated	
	Number	Average hospitalization period in days	Number	Average hospitalization period in days
Completely socially recovered	10	123	6	291
Socially recovered with psychic defects.....	2	146	2	179
Died from intercurrent diseases, not mental	1	170	3	192
Recovered after repeated hospitalization	3	116	6	185
Permanent relapse	2	110	1	377
Total	18	133	18	308

Here also there is a higher incidence of permanent pure remission in treated than in nontreated cases. The number of imperfect recoveries is the same for treated and untreated cases. On the other hand, the incidence of recidivations is lower in treated than in nontreated patients. The incidence of "recidivation" in nontreated cases corresponds to the figures given by Brodwall (1). Even if the material is too small to allow of conclusions as to whether there is a lower incidence of recidivation it can be concluded that the incidence is not higher in treated than in nontreated cases. The most striking difference, however, appears in the average hospitalization period per patient which for nontreated cases is more than twice that of cases treated.

Here, too, the same criteria are used as in the two other categories (schizophrenia and psychosis e constitutione), but under the same reserve as in psychosis e constitutione.

It is difficult to decide whether heredity on the whole and the

difference between the material and the control group presented here may play a part. The "duration of symptoms prior to admission" as well as "initial or recurrent phases" is about the same in both groups, a fact of particular importance regarding the manic-depressive psychosis (Braatøy (3), Lundquist (12), Stürup et al. (16)), whereas the distribution according to age varies. As in schizophrenia and psychosis the constitutione none of the treated patients are over the age of 55 for the simple reason that convulsion therapy has seldom been used in individuals who have reached this age. The patients treated are thus on the whole younger than the nontreated ones. In manic-depressive psychosis this according to Lundquist (12) might be considered an advantage, but the difference according to age in treated and nontreated patients is probably insignificant.

TABLE 16
Psychosis Manico-Melancholica.

	Treated					Nontreated				
Heredity	Familial occur.		No. fam. oc.			Familial occur.		No. fam. oc.		
	4		14			7		11		
Initial or recurrent phase	Initial		Recurrent			Initial		Recurrent		
	10		8			9		9		
Duration of symptoms on admission	I		II		III	I		II		III
	10		8		—	9		7		2
Age at the onset of the disease	—/25	—/35	—/45	—/55	Over 55	—/25	—/35	—/45	—/55	Over 55
	4	5	5	4	—	2	5	5	2	4

Based on the criteria previously mentioned the material of treated and nontreated cases is here also fairly homogenous, and as shown in the table the result is:

- a slightly higher incidence of permanent pure remissions and
- a definite shortening of the course of the disease in patients having undergone convulsion treatment.

CONCLUSION

- (1) The incidence of permanent pure remission in a material consisting of treated patients at least equals that in an adequate control material (from the same hospital and the same period) consisting of nontreated cases, or in other words: There is no higher incidence of recidivation in treated patients than in patients with spontaneous remission. This applies to patients discharged with the diagnoses schizophrenia, psychosis e constitutione, and manic-depressive psychosis.
- (2) The incidence of "socially recovered with psychic defects" is somewhat higher in nontreated patients. However, this applies only to patients discharged with the diagnosis schizophrenia or psychosis e constitutione.
- (3) The incidence of "permanent relapse" is the same in treated and in nontreated patients as concerns the three categories of mental disease mentioned.
- (4) The hospitalization period for patients receiving convulsion therapy has been reduced to $\frac{1}{2}$ to $\frac{1}{3}$ of that for nontreated patients.

According to articles 1-4 it seems justified to conclude that the convulsion therapy has contributed to a 100 per cent. increased capacity of Rønvik Hospital, this increase being a real one as shown in the first section of this paper.

On the basis of these facts and their considerable consequences concerning the sufferings of the individual patient as well as with a view to the public welfare (increased capacity of the hospital, a better utilization of hospital beds, i.e. an increased number of patients with the same number of beds, lower expenses per patient, and last but not least, the earlier return to normal activities and well-being of recovered patients) the convulsion therapy is not merely justifiable but even indicated in the mental disease here mentioned.

SUMMARY

A. The effect of the convulsion therapy at Rønvik Hospital has been studied and the following conclusions can be made:

- (1) That the capacity (circulation of patients) of the hospital has increased by about 100 per cent. per year since the use of convulsion therapy was adopted in 1939 and up to 1941, which was the last year of normal hospital activity.

- (2) That the average hospitalization period for discharged treated patients was 273 days and for discharged nontreated patients 839 days (average number of days per discharged patient).
- (3) That 447 patients were discharged during this four-year period, 215 treated and 232 nontreated cases. Of the treated patients 5.6 per cent. were discharged as "mental, not improved", while 35.3 per cent. of the nontreated patients discharged belonged to the same category. The remaining cases have been discharged as "not mental" or "mental, but improved", but these cases are considered as one group under the term "socially recovered".

B. A follow-up study has been carried out regarding 447 patients discharged during the period 1938-1941 (observation period 7 to 10 years). 88.3 per cent. of the questionnaires were answered. It appeared—regardless of the diagnosis at the time of the discharge—that:

- (1) The incidence of "permanent pure remission" is about 16 per cent. higher in treated than in nontreated cases.
- (2) The incidence of "socially recovered with mental defects" is 10 per cent. higher in treated than in nontreated cases.
- (3) The incidence of "permanent relapse" is practically the same in treated and in nontreated cases.

C. In order to determine whether the treated cases belonged to categories with a greater tendency to remission and better prognosis a "*diagnostic grouping*" of the material was carried out. It should be noted that the diagnosis both in treated and in nontreated cases was revised according to the patient's condition at the time of the discharge by the same physician all the time. Most of the discharged patients having undergone treatment (95 per cent.) belonged to the categories of schizophrenia, psychosis e constitutione, and manic-depressive psychosis. In the further investigation consideration has been given to patients discharged as "socially recovered" only according to the three categories mentioned (where the questionnaire has been answered).

120 treated and 36 nontreated cases of schizophrenia were discharged as "socially recovered". In this category there was:

- (1) 13 per cent. higher incidence of "pure permanent remission" in treated than in nontreated cases,
- (2) a slightly higher incidence of "recovered with psychic defects" in nontreated than in treated cases,

- (3) a higher incidence of "transient recurrence" in treated than in nontreated cases,
- (4) the same incidence of "permanent relapse" in treated and in nontreated cases,
- (5) a hospitalization period for treated cases of less than half that for nontreated cases.

D. In order to obtain a criterion for the severity of the disease the cases, treated as well as nontreated ones, have been investigated with a view to heredity, initial or recurrent phases of the disease, the duration of these phases prior to admission, and the age of the patient at the onset of the disease. The reason why other factors which may also play a part as to the evaluation have not been considered is commented on. The material as well as the control material evidently represents two adequate groups so that the result of the after-examination as shown in this paper seems reliable.

E. Except for some insignificant variations similar results are obtained and the same conclusion can be drawn as concerns patients discharged with the diagnosis psychosis e constitutione or manic-depressive psychosis.

On the basis of the result of this study it appears that the capacity of the hospital is increased by 100 per cent. per year, and that the increase is real and attributable to the convulsion therapy.

I wish to express my gratitude to my senior, Dr. G. Rohde Moe, for his permission to use the material from Rønvik Hospital and for all interest shown to this work. Further, I am obliged to my colleagues in Northern Norway who despite their being overloaded with work have provided valuable information for this study.

L I T E R A T U R E

From the extensive literature concerning shock therapy a selection is presented below, mainly comprising Scandinavian literature.

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DIE SENKUNGSREAKTION ALS QUANTITATIVE MESSMETHODE

Von
ERWIN HASCHÉ

Bei einer systematischen Untersuchung unseres psychiatrischen Krankenmaterials hinsichtlich der Abhängigkeit der Senkungsreaktion (SR) von dem Fibrinogengehalt des für die Senkungen benutzten Zitratplasmas ergibt sich Abb. 1. Für ca. 21 Fälle ist ein Zusammenhang zwischen SR und Fibrinogenmenge konstruierbar (s. Kurve in Abb. 1). Die Mehrzahl der Fälle — 36 —, in Abb. 1 umrahmt, fallen jedoch aus diesem Zusammenhang deutlich heraus. Schliesst man Senkungen grösser als 30 mm/h aus, da diese meist auf akute oder chronische Infekte zurückgehen, kann man sagen, dass — zumindest auf psychia-

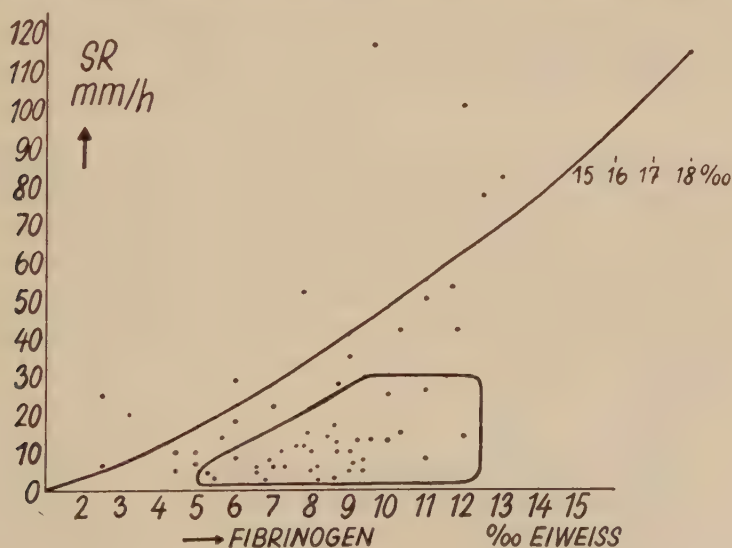


Abb. 1.

Senkung und Plasma-Fibrinogen, fotometrisch gemessen nach Aussalzung mit 27,4 %
Ammoniumsulfat in 11-facher Verdünnung.

trischem Gebiet — ein Zusammenhang zwischen SR und Fibrinogen *nicht existiert*. Dieses Ergebnis fordert zu einer neuerlichen Grundlagenuntersuchung der SR auf, da die bisherigen Untersuchungen über den Mechanismus der SR ergeben haben, dass für die Grösse der SR in der Hauptsache die Grösse der Fibrinogenfraktion des Plasmas verantwortlich sei.

Zuvor jedoch wurde untersucht, inwiefern man überhaupt die SR als quantitative Messmethode benutzen kann, da man weiss, dass sie teilweise mit recht grossen Fehlerquellen behaftet ist. Abb. 2 zeigt den typischen Verlauf der Senkung in Abhängigkeit von der Zeit unter verschiedenen Versuchsbedingungen. Bei Benutzung von Natriumzitrat

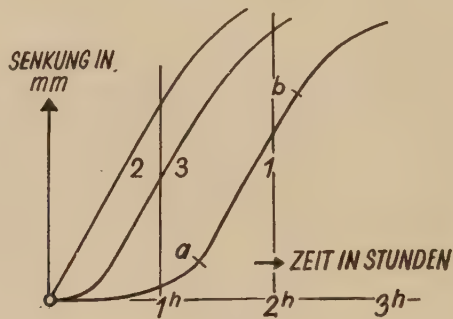


Abb. 2.

Typischer Senkungsverlauf unter verschiedenen Versuchsbedingungen.

- 1: 3,7 % Natriumzitrat 0,4 + Venenblut 1,6 in einem Rohr von 2 mm Durchmesser.
- 2: Dasselbe in einem Rohr von 9 mm Durchmesser.
- 3: 3 % Natriumfluorid 0,2 + Venenblut 1,8 in einem Rohr von 2 mm Durchmesser.

findet man zunächst eine Latenzzeit von 15—30 Minuten, während der keine Senkung erfolgt. Nach allmählicher Zunahme der Senkung folgt ein Bereich (von a bis b in Abb. 2), in dem die Senkung immer und in allen Fällen *mathematisch linear* ist. Danach folgt ein Bereich mit wieder abnehmenden Senkungswerten. Die Latenzzeit beruht nur zu geringen Teil auf Kapillarwirkung: benutzt man Natriumfluorid statt Natriumzitrat, so ist sie deutlich verringert (s. Abb. 2, Kurve 3). Da Natriumfluorid u. a. besonders die Thrombocyten schädigt, dürfte die Latenzzeit bei Natriumzitrat in erster Linie auf eine Thrombozytenwirkung zurückzuführen sein. Heparin ergibt dasselbe Verhalten wie Natriumzitrat. Durch Vergleich mit Kurve 2 erkennt man, dass das Stück a—b dem „wirklichen“ Senkungswert entspricht. Es sei jedoch darauf hingewiesen, dass die Kurve 2 — Senkung im 9 mm-Rohr — in einigen Fällen *steiler* verläuft als dem Stück a—b entspricht. Der mit a—b gefundene Senkungswert ist also ein *Mindestwert*.

Da es aus technischen Gründen nicht möglich ist, stets alle Senkungen bei quantitativen Messungen genau zu analysieren mit Feststellung des Kurvenstückes a—b, wird in folgendem versucht, Grundsätze aufzustellen, die es gestatten, auch ohne genaue Analyse quantitativ brauchbare Werte aus der Senkungsablesung zu gewinnen.

Es wurden zu diesem Zweck 135 Senkungen aller Grössenordnungen gemäss Abb. 2, Kurve 1 analysiert, der „wahre“ Wert W aus dem Verlauf des Kurvenstückes a—b bestimmt und dieser dividiert durch die Werte, die man bei Ablesung nach 1, 1½, 2 und 3 Stunden erhält.

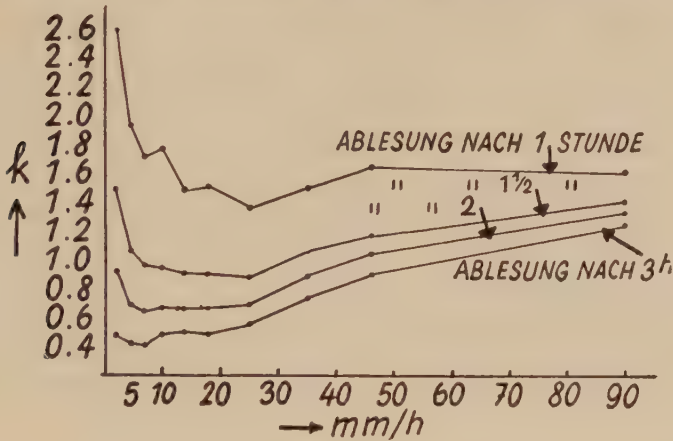


Abb. 3.

Tab. 1, dargestellt in Kurvenform.

k = Faktor, mit dem die resp. Ablesungswerte der Senkungen multipliziert werden müssen, um „wahre“ Werte zu erhalten.

TAB. 1

Beziehung des „wahren“ Senkungswertes W zu den Ablesungen nach verschiedenen Zeiten bei Benutzung von Zitratblut oder Heparinblut; (arithmetisches Mittel von je 10—20 Einzelwerten).

Senkung nach 1 Std. in mm	W_{1h}	$W_{1,5h}$	W_{2h}	W_{3h}
1—3	2,58	1,48	0,92	0,47
4—5	1,92	1,05	0,68	0,42
6—8	1,69	0,95	0,64	0,41
9—11	1,77	0,94	0,66	0,47
12—15	1,47	0,89	0,66	0,49
16—20	1,49	0,89	0,66	0,48
21—30	1,36	0,88	0,69	0,55
31—40	1,50	1,06	0,89	0,74
41—52	1,64	1,18	1,03	0,91
60—125	1,62	1,41	1,33	1,25

Diese Zahlen sind dann die Werte, mit denen man die respektiven Ablesungswerte der Senkungen multiplizieren muss, um in den einzelnen Fällen die „wahren“ Werte aus den Ablesungswerten zu erhalten. Als „wahrer“ Wert, bzw. Mindestwert gilt diejenige Anzahl Millimeter, die die betr. Senkung in 1 Stunde haben würde, wenn sie in dieser Zeit unverändert so fallen würde, wie es das Stück a—b angibt. In Tab. 1 sind die Ergebnisse dieser Analysen zusammengestellt. Für jede Zeile der Tab. 1 sind 10—20 Einzelbeobachtungen gemessen worden, welche arithmetisch gemittelt worden sind. Abb. 3 stellt die Ergebnisse in Kurvenform dar.

Es ergibt sich, dass die meist übliche Ablesung der Senkung nach 1 Stunde *besonders unzuverlässig* ist. Besonders in dem hier interessierenden Bereich der *kleinen* Senkungen ist eine ausserordentlich grosse Änderung des Umrechnungsfaktors für den „wahren“ Wert festzustellen, der den 1-Stundenwert als ungeeignet für quantitative Untersuchungen erscheinen lässt. Dem wahren Wert am nächsten liegt die Ablesung nach 1½ Stunde, wenn man von Senkungswerten kleiner als 4 mm/h und grösser als 40 mm/h absieht.

Um sich ein Bild von der Genauigkeit des *Einzelwerts* zu machen, sind in Tab. 2 die in den einzelnen Senkungsgruppen beobachteten *grössten* und (arithmetischen) *mittleren* Abweichungen für die Able-sungen nach 1 Stunde und nach 3 Stunden angegeben.

TAB. 2

Messgenauigkeit der Senkungsreaktion bei Benutzung von Zitrat- oder Heparinblut und Umrechnung auf „wahre“ Werte gemäss Tab. 1. — 10—20 Beobachtungen in jeder Reihe.

mm/h	1 ^h		3 ^h	
	Maxima	Mittel	Maxima	Mittel
1—3	+ 86 %, ÷ 51 %	± 28,6 %	+ 40 %, ÷ 19 %	± 10,6 %
16—20	+ 34 %, ÷ 28 %	± 17,0 %	+ 31 %, ÷ 27 %	± 12,5 %
42—52	+ 32 %, ÷ 45 %	± 22,4 %	+ 44 %, ÷ 70 %	± 28,4 %
60—100	+ 30 %, ÷ 35 %	± 15,4 %	+ 42 %, ÷ 64 %	± 30,2 %

Man sieht an den mittleren Abweichungen, dass für Senkungen bis 20 mm/h der Ablesungswert nach 3 Stunden sicherer ist ($\pm 10,6$ bis $\pm 12,5$ % gegenüber $\pm 17,0$ bis $\pm 28,6$ % bei Ablesung nach 1 Stunde). Für Senkungen über 40 mm/h ist dagegen der 1-Stundenwert sicherer. Im Mittelgebiet zwischen 20 und 40 mm/h sind beide Able-sungen ungefähr gleichwertig. Die Genauigkeit beträgt hier im Mittel

ca. $\pm 20\%$. Bei der einzelnen Messung können Fehler bis zu ca. $\pm 40\%$ vorkommen.

Fasst man Tab. 1 nach diesen Grundsätzen zusammen, so erhält man Tab. 3.

TAB. 3
Arbeitsvorschrift für quantitative Senkungsmessungen.

mm/h	Umrechnungsfaktor für »wahre« Mindestwerte bei Ablesung nach		Möglicher Fehler	
	1 ^h	3 ^h	Mittel	Maximum
bis 20	—	0,46	$\pm 12\%$	} ca. $\pm 40\%$
20—40	1,46	0,65	$\pm 20\%$	
über 40	1,61	—	$\pm 20\%$	

Alle diese Angaben gelten natürlich nur für Senkungen, die mit allen erforderlichen Vorsichtmassnahmen ausgeführt sind (trockene saubere Röhren, senkrechte Aufstellung, Vermeidung von Erhitzung durch Heizkörper oder Sonnenstrahlung, sofortige Messung, richtiges Zitratverhältnis, gute Mischung des Blutes, genaue Ablesung usw.).

ZUSAMMENFASSUNG

1. Auf dem Gebiet der Geisteskrankheiten findet man *keinen* Zusammenhang zwischen Fibrinogengehalt des Blutzitratplasmas und der Senkungsgeschwindigkeit der Erythrocyten desselben Plasmas. Man findet meist eine *Erhöhung* des Fibrinogen *ohne* Erhöhung der Senkung. In wenigen Fällen zeigte sich auch vermindertes Fibrinogen bei erhöhter Senkung.
2. Um mit der Senkungsreaktion quantitativ arbeiten zu können, müssen die beobachteten Werte mit einem Umrechnungsfaktor multipliziert werden (s. Tab. 3). Die so erhaltenen Werte sind *Mindestwerte*, da es sich gezeigt hat, dass die Senkung in manchen Fällen in weiteren Röhren als den üblichen grösser ist. (Vergleich der Senkung in Röhren von 9 mm und 2 mm Durchmesser). Der mittlere Fehler ist dann $\pm 20\%$ (maximal $\pm 40\%$).

SUMMARY

1. The sedimentationrate of the erythrocytes is independent from the fibrinogenrate of the plasma in psychiatric diseases.
2. When used as quantitative measurement, it is necessary to use the 3-hours-term in sedimentations untill 20 mm/h, multiplied with

0.46. Sedimentations greater than 20 mm/h can be measured quantitatively by the 1-hour-term, multiplied with the factor 1.61 (see Tab. 3). The standard-deviation is than $\pm 20\%$, the maximal deviation ca $\pm 40\%$.

SCHRIFTTUM

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ÜBER GERINNUNGSAKTIVE STOFFE UND DIE GERINNUNGSRELATION IN DER ZEREBROSPINALFLÜSSIGKEIT

Von

V. KAFKA

An anderem Orte (12) konnten wir feststellen, dass sich in der Zerebrospinalflüssigkeit (Zsp.) und zwar auch in der normalen gerinnungsaktive Stoffe finden. Da über dieses Gebiet, soweit uns bekannt ist, in der Litteratur kaum Andeutung zu finden sind, so konnten wir nicht auf solchen fussen, sondern mussten, um zu elementaren Resultaten zu kommen, eine grössere Reihe von Versuchsanordnungen kombinieren und neue ausfindig machen. So konnten wir zu Ergebnissen kommen, die schon ein gewisses Bild der Vorgänge boten. Die Beantwortung solcher Fragestellungen schien nicht unwichtig, denn sie konnten ein Licht auf die biologische Besonderheit der Zsp. werfen, es konnten sich Beziehungen besonders zu den Erkrankungen des Zentralnervensystems ergeben, und schliesslich war anzunehmen, dass einzelne der vielen schwebenden Fragen die Blutgerinnung (Ger.) betreffend vielleicht einer Klärung zugeführt könnten. In dieser Mitteilung nun haben wir uns die Aufgabe gestellt, unter Berücksichtigung der bisherigen Ergebnisse uns einer möglichst genauen Methodik zu bedienen, um so die bisherigen Feststellung, auf die wir noch eingehen werden, in einwandsfreier Weise zu vertiefen.

Die allgemeine *Technik* war folgende.. Die Versuche wurden zum grössten Teil in einem Wasserbad aus Glas vorgenommen, um die Ger. vorgänge auch während des Aufenthaltes der Röhrchen im Wasser genau beobachten zu können. Das Wasserbad wurde durch einen elektrischen Tachuwärmer und einen Thermoregulator stets bei der Temperatur von 37° C gehalten. Die Hinterwand des Wasserbades war mit schwarzem Papier beklebt, und das Wasserbad wurde von obenher beleuchtet. Diese Anordnung scheint uns besser als jene von *Astrup* (2), der durch ein gläsernes Wasserbad gegen einen hellen Gegenstand z. B. ein Fenster beobachtet. So war es für uns möglich, auch die schwächsten Grade von Opalescens, die in den Röhrchen auftraten zu beobachten. Die Röhrchen selbst wurden in Gestellen aufgenommen, die so eingerichtet waren, dass sie um ihre Horizontalachse nach links und rechts bewegt werden konnten. So war es möglich, den

Inhalt der Röhrrchen in Bewegung zu bringen ohne sie aus dem Wasser herausnehmen zu müssen. Die Beobachtung des Ger. eintrittes erfolgte also auf mehrere Arten: 1) Durch Beobachtung der Röhrrchen mit der Lupe, wodurch entweder das Auftreten von Opalescenz bei klarem Plasma oder das erste Erscheinen von Gerinnseln, 2) durch ein Bewegen der Röhrrchen, wodurch ein Festwerden der Flüssigkeit festgestellt werden konnte. Nebenbei sei bemerkt, dass uns die Beobachtung der ersten Opalescenz besonders zugute kam beim Arbeiten mit Citratplasma, das ja meist vollkommen klar ist. Zur Technik unserer Versuche sei weiter bemerkt, dass wir für unsere Oxalatplasmaversuche 9 ccm Blut in 1 ccm 2%ige Natriumoxalatlösung eintreten liessen, wobei wir uns graduiertes Zentrifugerröhrrchen bedienten. Für die Zitratplasmaversuche verwendeten wir meist die mit der *Westergren*-Spritze zur Ausführung der Senkungsreaktion entnommenen Blutproben (1,6 ccm Blut plus 0,4 ccm 3,8%iger Natriumcitratlösung). Alle Röhrrchen wurden gut geschüttelt und ca $\frac{3}{4}$ Stunden zentrifugiert. Bezüglich der Zentrifugierzeit sei auf das in der ersten Arbeit Gesagte hingewiesen. *Aggeler*, *Lucia-Howard* und *Mills* (1) haben zwar berichtet, dass keine Beziehungen zwischen Thrombocytenzahl und Ger. besteht, doch ist nach unseren Erfahrungen eine Beeinflussung der Ger. Zeit durch im Plasma noch vorhandene ev. lädierte Blutplättchen möglich. Auch *Owren* (16) vertritt diese Ansicht. Es wurde nur Plasma verwendet, dass nach Abgiessen von Blutkörperchen frei war. Vor dem Versuch wurden alle zur Verwendung kommenden Flüssigkeiten im Wasserbade vorgewärmt. Als CaCl_2 -Lösung wurde die von *Lehmann* (14) für die Prothrombinbestimmung vorgeschriebene 0,334%ige verwendet, die wir in fertiger Form von den Ferrosan-Werken bezogen. Das Gleiche gilt bezüglich der Thrombokinasen. Ferner liessen wir nach Zusatz der verschiedenen Flüssigkeiten immer eine Pause verstreichen, um eine gleichmässige Erwärmung der Gemische zu erreichen. Nach Zusatz der letzten Flüssigkeit wurde die Stopuhr in Gang gesetzt, und als Ger. Zeit wurde der Zeitraum gerechnet, der vom Zusatz der letzten Flüssigkeit bis zum Eintritt der ersten Ger. Erscheinungen verflossen war. Nach Beschickung der Röhrrchen wurden sie gut geschüttelt und dann in gleichen Zeitabständen bewegt. So brauchen die Röhrrchen nicht aus dem Wasser herausgenommen zu werden, und der Röhrrcheninhalt nicht durchgerührt zu werden, wie es verschiedene Methoden zur Prothrombinbestimmung vorschreiben. Die Beobachtung der ersten Ger. Erscheinungen erfolgte mit der Lupe und durch Bewegung der im Wasser befindlichen Röhrrchen. Die zur Verwendung kommenden Flüssigkeiten müssen natürlich möglichst klar sein, die Plasmen vor allem flockenfrei. Die Zsp. wurden selbstverständlich vorher genau untersucht. Zur Feststellung der Reaktionsfähigkeit der verwendeten Plasmen wurde den Versuchen eine Kontrolle mitgegeben, bei der die verwendete Plasmamenge durch die optimale Dosis der CaCl_2 -Lösung zur Ger. gebracht wurde. Bei der Anfertigung von Kurven bedienten wir uns meist der *reziproken* Ger. Zahl d. h. wir dividierten 100 durch die Ger. Zeit. Auch *Wöhlisch* (20) geht so vor, doch dividierte er 1, *Astrup* (2) 60 durch die Ger. Zeit. Als Material dienten die in der Anstalt entnommenen Zsp., sowie jene die uns von der neurologischen Klinik von Prof. *Antoni* zur Verfügung gestellt wurden, wofür auch an dieser Stelle der beste Dank ausgesprochen sei. Wir glauben mit der vorgetragenen Methode ein Optimum an Genauigkeit erzielt zu haben, besonders wenn die später zu besprechende Technik der Ger. Relation hinzukommt.

Bevor wir nun auf die mit dieser Methode erzielten Ergebnisse eingehen, seien kurz die wesentlichsten Resultate der früheren Ver-

suche resumiert. Es wurde gefunden, dass mit wenigen Ausnahmen jede Zsp. ger. aktiv sein kann. Es gibt jedoch Ausnahmen, die wir auch in den neuen Versuchen feststellen konnten und auf die später eingegangen werden wird. Bezüglich des Ausdruckes ger. aktiv sei gleich hervorgehoben, dass darunter eine Beschleunigung der Ger. des Systemes gegenüber der rekalkifizierten Kontrolle verstanden wird. Von Wichtigkeit ist die Beobachtung, dass alle Kategorien der Zsp., also Ventrikelflüssigkeit, Cysternen- und Lumballiquor ger. aktiv wirken können, die Ventrikelflüssigkeit vielleicht am stärksten. Diese Beobachtung könnte auch darauf zurückgeführt werden, dass manchmal der Calciumgehalt der Ventrikelflüssigkeit höher ist als in den anderen Liquorkategorien, doch ist das nur selten der Fall, und wir haben schon früher nachzuweisen versucht, dass der Calciumgehalt der Zsp. zwar für das Auftreten der Ger. Erscheinungen erforderlich ist, haben aber zur Evidenz gezeigt und werden in dieser Arbeit weitere Beweise dafür bringen, dass der Calciumgehalt nicht die Ursache der dargestellten Erscheinungen sein kann. Wir nehmen daher an, dass der Gehalt der Zsp. an Ger.aktiven Stoffen ihr schon bei ihrer Entstehung zugeteilt wird. Wir haben ferner beobachtet, dass Eetherschüttelung der Zsp. die Ger. des Magnesiumsulfatplasmas meist aufhebt, jene des Oxalatplasmas abschwächt, während mit Aether geschütteltes Serum in seiner Ger. Aktivität unbeeinflusst bleibt. Wird die Zsp. auf 56° erwärmt so bleibt die Ger. Aktivität gegenüber Magnesiumsulfatplasma meist ungeschwächt erhalten, während gegenüber Oxalatplasma die verschiedenen Zsp. different reagieren, d. h. sie werden entweder abgeschwächt, manchmal auch negativ, in anderen Fällen bleibt wieder die Ger. Aktivität erhalten. Auf 56° erhitzte Sera werden jedoch so gut wie immer ger.aktiv. Wird Magnesiumsulfatplasma mit Aether geschüttelt, so bleibt die Ger. Aktivität zugesetzter Zsp. unbeeinflusst, während die Rekalkifizierungskontrollen negativ werden. Wird Oxalatplasma nach *Bordet* (3) behandelt, so wird zugesetzte Zsp. ger. inaktiv, das Gleiche gilt von den Rekalkifizierungskontrollen, während zugesetztes Serum ger.aktiv bleibt. Wird Zsp. nach *Bordet* vorbehandelt, so wird ihre Ger. Aktivität abgeschwächt. Aus Versuchen mit Oxalatplasma ergab sich, dass Serumzusatz in *frischem* Zustand auf die Zsp. star ger. beschleunigend wirkt, während *altes* Serum die Ger. Aktivität herabsetzt. Aus diesen wesentlichen Ergebnissen, zusammengehalten mit einer Reihe anderer Beobachtungen, haben wir den Schluss gezogen, dass sich in der Zsp. Thrombokinase und Prothrombin nebeneinander vorfinden können, wenn auch vielleicht in anderer Form als im Blute.

In der ersten Arbeit haben wir als Ger. Zahl. der Zsp. die Ger. Zeit bezeichnet, die 1,5 ccm Zsp. an 0,1 ccm frischen normalen Oxalatplasmas bei 37° bewirkt. Diese Zahl war für Brutschranktemperatur angegeben und betrug im Mittel $22' \pm 6'24''$ für die Cysternen- und Lumbalflüssigkeit. Wie oben mitgeteilt, wurden die hier zu erörternden Versuche stets im Wasserbad bei 37° ausgeführt. Wir haben hier eine Mittelzahl für 2 ccm Zsp. berechnet, die 15'39" beträgt. Zieht man in Betracht, dass es sich hier um eine grössere Menge der Zsp. handelt, so ist der Unterschied gegenüber der früher berichteten Ger. Zahl nicht sehr gross. Für die Ventrikelflüssigkeit haben wir keine Mittelzahl gerechnet, weil uns zu wenige derartige Flüssigkeiten zu Gebote standen. Prinzipiell muss aber zu diesen Zahlen gesagt werden, dass sie kein genaues Bild der Ger. Verhältnisse der Zsp. geben können, da uns frische Zsp. nur in geringen Umfange zur Verfügung standen. Die meisten Flüssigkeiten waren mehrere Tage alt. Auch muss verlangt werden, dass das verwendete Plasma stets frisch ist und einem gesunden Menschen entstammt. Hier muss ausserdem bemerkt werden, dass eine Fehlerquelle darin liegt, dass der Kalkgehalt der Zsp. in wenn auch in nicht weiten Grenzen variieren kann. Wird daher so vorgegangen — worüber später noch zu berichten sein wird —, dass durch Natriumcitrat die endogene Ca-Wirkung ausgeschaltet und dann stets die gleiche Menge CaCl_2 -Lösung zugesetzt wird, so ergibt sich ein etwas niedrigerer Mittelwert und zwar 13'3" für 1,5 ccm Zsp. im Wasserbad bei 37°. Die erwähnten Zahlen sind zur Orientierung angegeben; sie besagen nur etwas, wenn sie zu der betreffenden Rekalzifizierungskontrolle in Beziehung gesetzt werden, worüber später ausführlich gesprochen werden wird.

Schon in der früheren Arbeit haben wir über Versuche berichtet, *die Wirkung des in der Zsp. vorhandenen Calciums auszuschalten*, indem wir zu der Zsp. Stoffe zusetzten, die nach dieser Richtung hin geprüft sind. Wir setzten sie zu der Zsp. in den gleichen Konzentrationen und Proportionen hinzu wie im Blute. Dabei machte sich die merkwürdige Beobachtung geltend, dass manchmal durch den hinzugesetzten Stoff auch später hinzugefügtes Calcium unwirksam gemacht wurde. In weiteren diesbezüglichen Versuchen nahmen wir darauf Rücksicht, dass die Calciumwerte der Zsp. nur die Hälfte der Blutwerte betragen, und dass vielleicht die Menge der wirksamen Calciums noch geringer ist. Wir gingen zuerst in der Weise vor, dass wir zu ca 5 ccm Zsp. eine Messerspitze Natriumfluorid zusetzten und nach einigen Zeit den so vorbehandelten Liquor in den Versuch einstellten und mit dem nativen verglichen. Es zeigte sich, dass auf diese Weise auch eine nachherige Calciumzugabe unwirksam gemacht wurde, und die Zsp. daher Ger.inaktiv blieb. In den folgenden Versuchen bedienten wir uns einer 3%igen Natriumfluoridlösung. In diesen Versuchen konnte festgestellt werden, dass 0,2 ccm der Natriumfluoridlösung die Ger. noch hemmte auch bei nachträglichem Calciumfluoridzusatz. Etwas Ähnliches war der Fall bei 0,1 und 0,05 der Natriumfluoridlösung. Dagegen konnten wir durch Zusatz von 0,03 ccm der Natriumfluoridlösung die Ger. Aktivität von 1,5 ccm der Zsp. hemmen,

doch trat hier nach Calciumzusatz wieder Ger. ein. Die besten Resultate nach dieser Richtung hin erhielten wir mit 3,8%iger Natriumzitratlösung. Hier zeigten die Menge von 0,2 0,15 und 0,1 ccm Hemmung der Ger. Aktivität auch nach späterem Calciumzusatz. Mit der Menge von 0,05 ccm jedoch konnte die Ger. Aktivität von 1,5 ccm Zsp. aufgehoben werden und nachfolgender Calciumzusatz war wirksam. Wie aus Tabelle 1 hervorgeht ist die Ger. Zeit der vorbehandelten und rekalkifizierten Zsp. meist kürzer als jene der nativen, doch kann sie auch gleich oder länger sein. Von wesentlicher Bedeutung aber ist hier der Vergleich des vorbehandelten und rekalkifizierten Zsp. Röhrchens mit dem rekalkifizierten Plasmaröhrchen. Nur in seltenen Fällen ist hier in letzterem die Ger. Zeit kürzer, fast überall ist sie länger, in vorbehandelten und rekalkifizierten Zsp. Röhrchen kürzer, wodurch der direkte Beweis erbracht ist, dass durch die Hinzufügung von Zsp. zum Plasma Ger. aktive Stoffe hinzukamen, dass also die Zsp. solche Stoffe enthält. Wir haben schon in der früheren Arbeit eine Reihe von Argumenten dafür angeführt, dass der Calciumgehalt der Zsp. zwar natürlich für die Ger. notwendig ist, diese aber nur durch die Mitwirkung der in der Zsp. vorhandenen Ger. aktiven Stoffe zustande kommt. Durch diese Versuchsanordnung die wir *Ger. Relationen* nennen, ist auch eine grundlegende Technik für weitere Versuche geschaffen. Sie war, wie auch Tabelle 1 zeigt, die folgende: Es wurde die native Zsp. in der Menge von 1,5 ccm (evtl., abhängig von der zur Verfügung stehenden Menge, 1,0 oder 2,0 ccm) als erstes Röhrchen angesetzt, als zweites die mit 0,5 ccm der 3,8%igen Natriumzitratlösung versehene Zsp. in derselben Menge, als drittes Röhrchen ebenfalls 1,5 Zsp. die vorher citriert und nachher mit 0,1 ccm der 0,334%igen CaCl_2 -Lösung versehen war. Alle Röhrchen erhalten 0,1 ccm des Citratplasmas. Als viertes Röhrchen figurierte das mit derselben Calciumchloridlösung versehene Citratplasma. Alle Röhrchen waren mit 0,8%iger Kochsalzlösung auf das gleiche Volumen aufgefüllt. Das zweite Röhrchen des Versuches soll natürlich während der ganzen Versuchsdauer keine Ger. aufweisen. Das wird meist mit 0,05 ccm Natriumzitratlösung erreicht. Nur in zwei Fällen der Tabelle wurden höhere Mengen verwendet. Bedenklich erscheint es dass in einigen Fällen besteht die freilich geringe Gefahr, dass die Citratmenge nicht die Gesamtmenge des endogenen Calciums unwirksam gemacht hat, und daher das Röhrchen 3 nicht genau anzeigt. Vergleichversuche haben uns jedoch gezeigt, dass dieser Fehler sehr gering ist. Es ist sehr interessant, dass selbst in den Fällen, wo das Plasma sich nicht rekalkifizieren liess, in der citrierten Zsp. die ohne Calcium keine Ger. Aktivität mehr aufwies, nach Ca-Zusatz Ger. auftrat und zwar oft

TABELLE 1.
Gerinnungsrelation des Oxalatplasmas. Index.

Versuchs- Nr.	Liquor		Oxalat- plasma 0.1 ml Alter	Natr. citr. 3.8 % Menge	Gerinnungszeit				Index a · 100 b	CaCl ₂ % Menge ml	Bemerkung	
	Nr.	Menge ml			Alter	1 Liquor nativ	2 Liquor citriert	3 (b) Liquor citriert + CaCl ₂				4 (a) Recalc. Kontr.
324	79	1.5	2 T.	4 T.	0.05	60'	×	31'30"	Fl.	—	0.1	
329	93	1.5	3 T.	5 T.	0.05	12'	×	12'	Fl.	—	0.1	
330	92	1.5	5 T.	frisch	0.05	22'20"	n. T.	15'	10'30"	68	0.1	
331	99	1.5	2 T.	2 T.	0.05	8'	n. T.	8'	22' p.	270	0.1	
332	101	1.5	1 T.	3 T.	0.05	5'40"	Fl.	6'30"	7' 5"	119	0.1	
333	102	1.5	2 T.	4 T.	0.05	7'40"	×	8'	10'	125	0.2	
334	100	1.5	3 T.	5 T.	0.07	10'20"	n. T.	17'20"	27'	156	0.15	
336	105	1.5	2 T.	2 T.	0.05	6'40"	n. T.	ca. 15'	6'40"	42	0.1	
337	108	1.5	1 T.	3 T.	0.05	11'20"	×	40'	Fl.	—	0.1	
338	106	1.5	3 T.	4 T.	0.05	10'45"	×	8'10"	10'20"	124	0.1	
342	112	1.5	2 T.	3 T.	0.05	8'20"	×	9'3 "	n. T.	—	0.1	Recalc. Kontr. + Thrombokin. 14'40"
343	114	1.5	3 T.	4 T.	0.05	7'15"	n. T.	6'35"	n. T.	—	0.1	Recalc. Kontr. + Thrombokin. 23'
344	116	1.5	1 T.	1 T.	0.05	4'45"	×	5'	7'	140	0.1	
345	115	1.5	4 T.	4 T.	0.05	5'50"	×	5'50"	×	—	0.1	

349	123	1.5	1 T.	1 T.	0.05	6'30"	n. T.	7'50"	n. T.	—	0.1
351	127	1.0	3 T.	4 T.	0.05	8'20"	×	4'45"	21'	470	0.2
353	132	1.0	1 T.	8 T.	0.05	21'	×	15'30"	78'	509	0.2
354	133	1.0	2 T.	9 T.	0.05	ca. 55'	×	14'	61' p.	435	0.2
355	135	1.0	2 T.	1 T.	0.05	15'	n. T.	6'20"	8'5"	137	0.2
357	136	1.0	4 T.	3 T.	0.05	18'	×	9'	12'15"	135	0.2
358	139	1.0	3 T.	7 T.	0.05	18'30"	×	9'30"	36'	387	0.2
360	150	1.0	1 T.	5 T.	0.05	15'50"	×	6'50"	19'	292	0.2
361	151	1.0	2 T.	8 T.	0.05	n. T.	×	11'	87'	790	0.2
362	152	2.0	3 T.	9 T.	0.1	12'	×	12'	ca. 300'	—	0.2
363	153	1.5	5 T.	11 T.	0.05	16'	×	12'	n. T.	—	0.2
364	154	1.0	7 T.	1 T.	0.05	6'20"	×	4'	6'55"	163	0.2
366	161	1.0	2 T.	11 T.	0.05	×	×	×	16'	—	0.2
367	165	1.0	1 T.	1 T.	0.05	×	×	5'20"	5'20"	100	0.2
373	176	1.0	2 T.	7 T.	0.05	4'40"	×	7'	12'	171	0.1
374	185	1.0	4 T.	22 T.	0.05	×	×	×	23'	—	0.1
380	290	1.0	2 T.	3 T.	0.05	×	×	×	31'	—	0.1
381	2	1.0	1 T.	frisch	0.05	n. T. ?	×	Fl.	6'25"	—	0.1

T. = Tage.

n. T. = Ger. tritt am nächsten Tage ein.

× = Kein Ger. innerhalb der Versuchsdauer.

Fl. = Flockung.

p. = partiell.

Dem. paralytica
Lues cerebriDem. paralytica
Dem. paralytica
Dem. paralyticabeh.

schon früher als in den ersten Röhrchen, also der native Zsp. Gerade aus solchen Ergebnissen ersehen wir deutlich die Einwirkung der Ger. aktiven Stoffe der Zsp. Eine Analyse solcher Versuche ergibt also um es noch einmal hervorzuheben, folgendes Bild: Aus dem ersten Röhrchen bekommen wir ein Bild über die Ger. Aktivität der nativen Zsp. wobei freilich der nicht immer gleiche Ca-Gehalt der Zsp. interferiert. Das zweite Röhrchen zeigt uns, ob der Citratzusatz genügend gross war, um die Ca-Wirkung vollständig auszuschalten. Das dritte Röhrchen muss vor allem mit dem vierten verglichen werden und zeigt uns wenn die Ger. in ihm stärker beschleunigt ist, die Ger. Aktivität der Zsp. an, freilich exakt nur dann, wenn das zweite Röhrchen innerhalb der Versuchsdauer keine Ger. zeigt. Ein Vergleich des dritten mit dem ersten Röhrchen ist dann interessant, wenn die Ger. im dritten Röhrchen schneller abläuft als im ersten. In solchen Fällen war der normale Calziumgehalt der Zsp. wohl nicht optimal für die Entstehung der Ger. Wir haben uns nun bemüht, einen zahlenmässigen Ausdruck für die Stärke der Ger. Aktivität der Zsp. zu finden. Es geschah das ähnlich wie bei der *Quick-Lehmannschen* Prothrombinbestimmung. Wir haben zu dem Zweck die Ger. Zeit der Rekalzifizierungskontrolle mit 100 multipliziert und durch die Ger. Zeit der citrierten und rekalzifizierten Zsp. dividiert, also entsprechend der Tabelle $\frac{a \cdot 100}{b}$.

Die so erhaltenen Werte geben,, wenn sie über 100 sind, ein gutes Bild der Ger. Aktivität der Zsp. Sind die Zahlen unter 100, so wird eine antithrombische Wirkung der Zsp. oder eine andere Ger. Hemmung aufgezeigt. Ist der Index 100, zeigen also Röhrchen 3 und 4 den gleichen Wert, so hat sich die Zsp. Ger. neutral verhalten. Auf diese Punkte wird noch ausführlich einzugehen sein. Eine Indexberechnung ist natürlich nicht möglich, wenn die Rekalzifizierungskontrolle innerhalb der Versuchszeit keine Ger. zeigt. Auch werden die Indexwerte sehr hoch, wenn die Ger. der Rekalzifizierungskontrolle erst nach mehreren Stunden statthat. Die Indexberechnung ist daher in erster Linie bei frischen Plasmen zu verwenden, da die Indexwerte bei Abnahme der Ger. Fähigkeit des Plasmas natürlich ansteigen. Wir haben ja schon früher gezeigt, wie schnell z. Bsp. Oxalplasma Ger. inaktiv werden kann, dass es aber durch die Zsp. trotzdem aktiviert wird, wodurch das „Kreuzphänomen“ entsteht. Zu relativ exakten werten kommt man also nur, when es sich um ein Plasma handelt, das nicht über 48 Stunden alt ist. Haben doch auch *Dyckerhoff*, von *Behm*, *Goossens* und *Miehler* (6) festgestellt, dass die Rekalzifizierung des Plasmas innerhalb der ersten 48 Stunden konstante Ger. Werte ergibt. Sonst hat die Indexberechnung nur theoretischen Wert, aber der

Vergleich der Rekalzifizierungskontrollen älterer Plasmen mit den citrierten und rekalzifizierten Proben der Zsp. kann uns besonders deutlich die Ger. Wirksamkeit der Zsp. aufzeigen.

Eine genauere Betrachtung der Tabelle 1 besagt noch das folgende: In Nr. 1 der nummerierten Spalten sehen wir die Ger. Zeiten der nativen Zsp. Sie zeigen eine gewisse Buntheit, was darauf zurückzuführen ist, dass die Zsp. ein verschiedenes Alter hatten, ferner waren auch die verwendeten Oxalatplasmen nicht gleichaltrig., schliesslich differiert vielleicht auch der native Ca-Gehalt der Zsp. Die zweite Spalte besagt, ob die verwendete Citratmenge ausreichend war. Die dritte Spalte zeigt die Ger. Zeit der rekalzifizierten und vorher citrierten Zsp., die einwandfrei ist, wenn in Spalte 2 das Ergebnis negativ war. Spalte 4 weist die Ger. Zeit des rekalzifizierten Plasmas auf. Aus den Ergebnissen der Spalte 3 und 4 wird der Ger. Index der Zsp. berechnet. Noch ein Wort über die zur Rekalzifizierung verwendete CaCl_2 -Menge. Über diese Frage hat sich neben vielen anderen *J Lehmann* (14) ausführlich geäussert. Er sieht als optimal für seine Methode der Prothrombinbestimmung 0,1 ccm der 0,334 % igen CaCl_2 -Lösung an. Es handelt sich hier aber um Citratplasma. Wie aus unserer Tabelle 1 hervorgeht, haben wir sowohl mit 0,1 wie mit 0,2 ccm der 0,334 % igen CaCl_2 -Lösung gute Resultate erhalten. Die Hauptsache ist die gleichmässige Rekalzifizierung der beiden Röhrchen und die Vermeidung eines sicheren Unter- oder Überschusses der CaCl_2 -Lösung. Worauf die Verzögerung der Ger. In Spalte 3 gegenüber in Spalte 1 zurückzuführen ist, wie sie sich in den Versuchen 334, 336, 337 und in schwächerem Masse 342 zeigt, ist schwer zu sagen, vielleicht ist es der höhere Ca-Gehalt der nativen Zsp. In den Versuchen 334 und 336 war übrigens, wie Spalte 2 zeigt, die Citrierung nicht ganz ausreichend. Über jene Versuche, bei denen das Resultat der Spalte 3 eine längere Ger. Zeit angezeigt hatte, als jenes der Spalte 4, wo also der Index unter 100 lag, wird anlässlich der Frage der antithrombischen Wirkung der Zsp. noch zu sprechen sein. Besonderes Interesse aber beanspruchen noch die Fälle, bei denen die Rekalzifizierungskontrolle Ger. zeigt, die Röhrchen mit Zsp. dagegen nicht, wie die Versuche 336, 374 und 380 der Tabelle 1. Hier ist wohl keine antithrombische Wirkung anzunehmen, sondern eine *Hirschfeld-Klinger-sche* Reaktion (10), wie sie besonders von *Carlinforti* (4,5) für die Zsp. beschreiben worden ist. In einer grösseren Arbeit über dieses Thema äussert sich *Carlinforti* folgendermassen: „Es scheint nach diesen Versuchen nicht mehr zweifelhaft, dass bei der Syphilis die positive Ger. Reaktion (d. h. die Hemmung der Ger. Ref.) durch die Bindung der in den alkoholischen Organextrakten enthaltenen Haptene

durch spezifische Antikörper des Serums zustande kommt, also nicht als ein lediglich physikalisch bedingtes Phänomen zu betrachten ist.“ Dieselbe Ansicht äussert *Carlinforti* auch bezüglich der Zsp. Man lässt die Zsp. zuerst mit dem Organextrakt als zusammentreten. Nach einer Stunde wird Serozym (Oxalatplasma rekalkifiziert und das bei der Ger. ausgeschiedene Serum als Serozym verwendet) hinzugesetzt und die CaCl₂ Lösung, nach weiteren fünf Minuten erfolgt der Zusatz des verdünnten Oxaloplasmas. Je nach der Verzögerung des Eintritts der Ger. gegenüber der Kontrolle wird die Stärke der Reaktion bestimmt. *Carlinforti* nimmt an, dass diese Methode empfindlicher als die WaR ist, aber sie ist nicht vollständig spezifisch. Es ist nun nicht unmöglich, dass unseren Beobachtungen ein ähnlicher Mechanismus zugrunde liegt, dass also durch die in der Zsp. vorhandenen Reagine die Wirksamkeit der in der Zsp. und im Oxalatplasma vorhandenen Thrombokinase (Cytozym) gehemmt wird. Es ist ja auffallend, dass unter den 34 untersuchten Fällen der Tabelle 1 es gerade die Paralysen waren, die dieses Phänomen am deutlichsten zeigten. In Versuch 367 handelt es sich um eine Lues cerebri. Da hier das citrierte und rekalkifizierte Zsp.-Rörchen dieselbe Ger. zeigt wie die Rekalkifizierungskontrolle, scheint nur die Thrombokinase der Zsp. unwirksam gemacht zu sein. Interessant ist auch der Versuch 381, der das Phänomen in abgeschwächter Form gibt. Es handelt sich um eine behandelte Paralyse. Wie weit die besprochene Erscheinung praktische Bedeutung hat, lässt sich noch nicht genau sagen, da nicht genug Fälle untersucht worden sind. Man benötigt ja zur Ausführung eines Versuches 4,5 ccm Zsp., da unter 1,5 ccm pro Rörchen am besten nicht heruntergegangen werden soll. Zu betonen ist, dass das Phänomen sich anscheinend nur mit Oxalatplasma erzielen lässt; mit Citratplasma erhält man keine so eindeutigen Ergebnisse, soweit unsere bisherigen orientierenden Versuche zeigen, und mit Magnesiumsulfatplasma erscheinen sogar, wie ich in einer früheren Arbeit berichtet habe, entgegengesetzte Resultate (deutliche Ger. Aktivität gerade bei Paralysen). Es liegt hier anscheinend ähnlich wie bei der von *Fuchs* (9) angeschnittenen Frage: Prathrombin-Komplementmittelstück ein reizvolles Grenzgebiet zur Immunitätsforschung vor. Aus der neuen Versuchsanordnung der Ger. Relation lassen sich also drei Dinge ablesen, wie zusammenfassend gesagt sei: 1) Die Stärke der Ger. Aktivität der Zsp., die sich daraus ergibt, wie weit der Index über 100 gestiegen ist, 2) eine antithrombische Wirkung wenn der Index unter 100 sinkt, 3) eine hier besonders verlaufende *Hirschfeld-Klingersche* Reaktion. In einer Reihe von Versuchen liess sich der Index nicht aufstellen, weil die Rekalkifizierungskontrollen versagten.

Im Verlaufe der weiteren Versuche hatten wir zum Ziele, die *Technik* der Ger. Relation der Zsp. besonders genau zu machen und sie zu vereinfachen. Versuche, die Haemosallösung der Astra-Werke wegen ihres Salzgehaltes als Kontrollflüssigkeit zu benützen, hatten nicht das gewünschte Resultat. Dagegen schien es uns notwendig, in ähnlicher Weise, wie *Owren* (16) vorgegangen ist, die Gemische zu puffern. Zu diesem Zwecke wurde so vorgegangen, dass wir 285 ccm einer 1,7 %igen Veronallösung mit 215 ccm n/10 HCL und 2,83 g NaCl versetzen und auf 500 ccm mit 0,9 %iger Kochsalzlösung auflösen. Von dieser Lösung setzten wir 0,5 ccm zu jeden Versuchsröhrchen. Es zeigte sich nun, dass die Rekalzifizierungskontrollen die gleiche Ger. Zeit zeigten, gleichgültig ob sie mit Puffer versetzt oder nicht. Die Erklärung war die, dass sowohl die gepufferten wie die nichtgepufferten Proben die gleiche pH aufwiesen. Dagegen zeigten die Liquorröhrchen meist eine grössere Ger. Beschleunigung, wenn sie gepuffert waren. Die Ursache dieser Erscheinung war in einem Anwachsen von pH nach der alkalischen Seite zu suchen, die sich bei den nichtgepufferten Röhrchen meist zeigte. Bevor wir auf diesen Punkt näher eingehen, seien weitere Modifikationen der Technik besprochen. Hatten wir durch den Natriumcitratzusatz versucht den nativen Calciumgehalt der Zsp. unwirksam zu machen, so musste weiter um die Kontrolle der Zsp. möglichst ähnlich zu machen, die 0,9 %ige Kochsalzlösung mit soviel Calciumchloridlösung versetzt werden, dass sie ungefähr dem Calciumwert der Zsp. entsprach. Nach unseren Berechnungen war, wenn wir von 1,5 ccm Zsp. ausgingen, 0,02 ccm der 0,334 %igen Cl_2 -Lösung auf 1,5 ccm Kochsalzlösung nötig. Wir haben diese neue Versuchsanordnung an vielen Zsp. versucht und sie ausgezeichnet funktionierend gefunden. Wir haben sie die *abgekürzte Ger. Relation* genannt deswegen, weil die Röhrchen 1 und 2 der früher erwähnten Ger. Relation weggelassen konnten. Die Indexberechnung erfolgte wie schon erwähnt in der Weise, dass die Ger. Zeit der Rekalzifizierungskontrolle mit 100 multipliziert und durch die Ger. Zeit des Liquor-Röhrchens dividiert wurde. Es sei hier noch einmal die Technik dieser abgekürzten Ger. Relation mitgeteilt. Es werden zwei Röhrchen angesetzt und das eine mit 1,5 ccm Zsp. das andere mit 1,5 ccm 0,9 %iger Kochsalzlösung versetzt. Zu den ersten Röhrchen kommt 0,02 ccm der 0,9 %igen Kochsalzlösung, zu dem zweiten Röhrchen 0,02 der 0,334 %igen CaCl_2 -Lösung. Des weiteren wird zu beiden Röhrchen 0,05 ccm der 3,8 %igen Natriumcitratlösung hinzugesetzt. Hierauf kommt 0,1 ccm Plasma hinzu. Als Plasma wurde späterhin nur Citratplasma verwendet, das von dem zur Senkungsreaktion geschickten Blut abgehoben war. Wir verwendeten Misch-

plasma, weil hier die in der früheren Arbeit beschriebenen individuellen Eigenschaften der Plasma keine Rolle spielten. In vielen Versuchen wurde jetzt aus später zu erörternden Gründen pH bestimmt. Natürlich waren alle Flüssigkeiten vorgewärmt und man liess vor Zusatz einer neuen Flüssigkeit einige Minuten vergehen zur weiteren Durchwärmung der Gemische im Thermostaten. Zum Schlusse wurde die Calciumchloridlösung in der Menge von 0,1 ccm zugesetzt. Auch sie war natürlich vorgewärmt. Die Ger. Zeit bei jedem Röhrchen einzeln bestimmt, und zwar von dem Moment des Zusatzes der Calciumchloridlösung bis zu dem Auftreten der ersten Ger. Erscheinungen, wobei keine Rücksicht darauf genommen wurde, welche Form das auftretende Gerinnsel hatte. Mit dieser Technik hatten wir nun wie Tabelle 2 zeigt mit den meisten Proben der Zsp. Ergebnisse mit einem Index über 100, die also deutlich und einwandfrei die Ger. fördernde Wirkung der Zsp. aufzeigten. Wir glauben mit dieser Versuchsanordnung einen optimalen Grad von Genauigkeit erreicht zu haben bei relativ einfacher Technik. Zu weiteren Überlegungen aber regten die Fälle an, bei denen der Index unter 100 geblieben war. Lag hier eine antithrombische Wirkung vor oder was war anzunehmen? Schon in Tabelle 1 war in den Versuchen 330 und 336 ein ganz besonders niedriger Index zu beobachten. Wir möchten daher an dieser Stelle auf die Ansichten zu sprechen kommen, wie sie von *Wöhlisch* und *Grüning* (21) und anderen über die Antithrombinwirkung geäussert worden sind. *Rettger* (18) hat als erster angenommen, dass das spontane Verschwinden des Thrombins im Normalserum vielleicht auf einer Bindung des Thrombins an einen Serumeiweisskörper beruht. Das Serum wäre also befähigt, die Aktivität des Thrombins wie andere Fermentwirkungen aufzuheben. Das Metathrombin würde dann aus an Serum gebundenen und dadurch inaktiviertem Thrombin bestehen, wofür auch die Beobachtung *Landsbergs* (13) spricht, der diese Bindung durch Alkali wieder sprengen konnte. *Quick* (17) hat dann durch interessante Versuche nachgewiesen, dass durch Kontakt des Albumins mit dem Thrombin die Ger. Zeit. hundertfach verlängert wird, während das Globulin die Ger. Zeit nur verdoppelt. *Wöhlisch* und *Grüning* (21) haben nun eingehende Versuche gemacht und die Angaben *Quicks* (17) vollinhaltlich bestätigt. Erwähnenswert ist, dass nach diesen Verfassern die Hemmung durch Albumin mit höheren Temperaturen wächst, ebenso (bis zu einem Maximum) mit steigender Albumin- und fallender Thrombinkonzentration. Die Einwirkung des Globulins ist sehr gering. Auf Grund dieser Versuche wäre es denkbar, dass in der Zsp. nach dieser Richtung hin ganz besonders günstige Verhältnisse herrschen. Der Globulinalbuminquotient

TABELLE 2
Abgekürzte Gerrelation.

Datum	Versuchs Nr.	Liquor vom	Liquor Nr.	Citratplasma vom	Ger. zeit	Ger. zeit der Kontrolle	Index	Bemerkung
10—1—48	637		158		15'	90'	600	
13—1—48	638		159		n. T.	90'		
			164		×	n. T.		
			165		n. T.	n. T.		
24—1—48	640	10—1—48	166		25'	n. T.	ca. 2400	
28—1—48	641	21—1—48	3	21—1—48	24'	n. T.	ca. 1350	
20—2—48	643	7—1—48	4	21—1—48	32'	n. T.	ca. 1870	
2—3—48	645	17—2—48	11	27—1—48	10'	100'	1000	
		2—3—48	12	10—2—48	n. T.	×		
26—4—48	651	26—4—48	17	a) 2—3—48	8'	n. T.	ca. 7500	
14—5—48	652	7—5—48	18	b) 2—3—48	10'	n. T.	ca. 6000	
		12—5—48	19	17—4—48	78'	n. T.	ca. 760	
		12—5—48	20	12—5—48	n. T.	×		
14—8—48	656	20—8—48	37	12—5—48	n. T.	×		
21—8—48	657	20—8—48	39	11—8—48	20'	n. T.	ca. 3000	mit und ohne Puffer
		17—9—48	44	11—8—48	18'	36'	200	mit Puffer
1—10—48	659	29—9—48	45	11—8—48	21'	36'	171	
				28—9—48	4'	22'	550	mit Puffer
				28—9—48	12'	22'	183	

n. T. = Ger. am nächsten Tag beobachtet.

×

der normalen Lumbalflüssigkeit ist nämlich 0,1 bis 0,4 wobei aber Zahlen um 0,25 am häufigsten vorkommen. Im Serum ist dieser Quotient höher, nämlich 0,33 bis 0,6. Die Zsp. ist also *relativ* albuminreicher als das Blutserum, und es wäre daher denkbar, dass die die Ger. Aktivität hemmende Albuminwirkung sich hier deutlicher äussern kann als im Serum. Wir haben daher die in den Versuchen 330 und 336 der Tabelle 1 verwendeten Zsp. auf ihren Gehalt an Globulin und Albumin untersucht, wie wir es mit Hilfe der Eiweissrelation in allen solchen Fällen machen. Die Werte folgende:

Vers. 330, Zsp. 92: Ges. Eiw. 1,1, Glob. 0,15, Alb. 0,95, Qu. 0,15.

Vers. 336, Zsp. 105: Ges. Eiw. 1,2, Glob. 0,55, Alb. 0,65, Qu. 0,84.

Ges. Eiw., Glob. und Alb. in Teilstrichen.

Während also die erste Flüssigkeit relativ albuminreich ist, ist die andere relativ albuminarm. Trotzdem haben beide Flüssigkeiten antithrombische Wirkungen. Es scheint, daher nicht wahrscheinlich zu sein, dass ein Überschuss an Albuminen oder die Eiweisskörper überhaupt eine Rolle bei der Herabsetzung des Ger. Index spielt.

Wir waren also genötigt andere Erklärungen für die scheinbar antithrombische Wirkung einzelner Zsp. zu finden. Führend dabei waren die Pufferversuche, die ja eine deutliche Herabsetzung der Ger. Zeit anzeigten. Durch die Pufferung aber wurde die alkalische Reaktion der Zsp. auf ungefähr $\text{pH} = 7,4$ gebracht. *Astrup* (2) hatte ja mitgeteilt, dass für das Thrombin sich eine optimale Stärke von pH finde. Auch *Owren* (16) zeigt in seinem Buche eine Kurve, aus der hervorgeht, dass für den Ablauf des Ger. Vorganges sich ein Optimum bei ungefähr $\text{pH} = 7$ findet, während bei 6 und 8 die Ger. Zeiten sich deutlich verlängern. Wir hatten auf diesen Faktor früher nicht genügend Rücksicht genommen, weil uns in Versuchen, die wir in der ersten Mittellung schilderten, eine wesentliche Einflussnahme von pH auf die Ger. Zeit nicht aufgefallen war. Es hatte sich aber dabei um Versuche gehandelt deren Technik noch etwas primitiv war; es handelt sich um Oxalatplasma, und die Ger. Zeit wurde bei Zimmertemperatur abgelesen. Immerhin ist schon in diesen Versuchen gewisse Tendenz zu langen Ger. Zeiten bei hohen pH -Werten zu sehen. Einen Versuch der die starke Einwirkung von pH auf die Ger. Zeit, deutlich demonstriert finden wir in Tabelle 3. Hier waren wir in der Weise vorgegangen, dass wir eine 11 Tage alte aber noch klare Zsp. in die abgekürzte Ger. Relation einstellten, und zwar in der Menge von 1,5 ccm. Die Ger. dieses Liquorgemisches trat erst am nächsten Tage auf, jene der Kontrolle schon nach 8 Minuten 55 Sek. Wir bestimmten

TABELLE 3.

Endgiltige Technik der abgekürzten Ger.relation.

Datum	5 ₄ 49	5 ₄	5 ₄	9 ₄	9 ₄	9 ₄
Versuch Nr.	670		670	671		671
Liquor Nr. u. Menge	10	1.5	—	11	1.5	—
CaCl ₂ Lös.			0.02			0.02
NaCl 0.9 %		0.02	1.5		0.02	1.5
Natr. citr. 3.8 % . . .		0.05	0.05		0.05	0.05
Citratplasma 29/3 . .		0.1	0.1		0.1	0.1
pH		8.5	7.5		8.5	7.5
n/10 HCl		4Tr.	4Tr.		4Tr.	4Tr.
		0.9 % NaCl.			0.9 % NaCl.	
CaCl ₂ Lös.		0.1	0.1		0.1	0.1
Ger.zeit		9'15"	32'		9'45"	22'10"
Index		343			233	

TABELLE 3.

Bedeutung von pH.

Datum	23 ₃	24 ₃	24 ₃	24 ₃	26 ₃	26 ₃
Versuch Nr.	667	667	668	668	669	669
Liquor 8	1.5		2.0		1.5	
CaCl ₂ Lös.		0.02		0.02		0.02
NaCl 0.9 %	0.02	1.5	0.02	1.5	0.02	1.5
Natr. citr. 3.8 % . . .	0.05	0.05	0.05	0.05	0.05	0.05
Citratplasma 21/3 . .	0.1	0.1	0.1	0.1	0.1	0.1
pH	8.5	7.2	7.3	7.3	7.5	7.5
CaCl ₂ Lös.	0.1	0	0.1	0.1	0.1	0.1
Ger.zeit	n. T.	8'55"	7'	22'	8'30"	30'
Index	ca. 0.01		314		361	

nun pH der beiden Versuchsgemische und musten konstatieren, dass das Zsp. Röhrchen pH = 8,5 hatte, das Kontrollröhrchen pH = 7,2. Am nächsten Tage gingen wir nun so vor, dass wir die gleiche Versuchsanordnung mit der Menge von 2 ccm Zsp. ansetzen. Vor Zusatz der Calciumchloridlösung massen wir pH und fanden die Zahlen 8,5 für das Liquorröhrchen und 7,3 für die Kontrolle. Wir setzen nun zu dem Röhrchen mit Zsp. 4 Tropfen $\frac{1}{10}$ n HCl und zu dem Kontrollröhrchen 4 Tropfen Kochsalzlösung. Beide Gemische zeigten nun pH = 7,3. Hierauf wurde die Calciumchloridlösung zugesetzt. Die Ger. Zeit des Zsp. Röhrchens war nun 7 Minuten jene der Kontrolle 22

Minuten, was einem Ger. Index der Zsp. von 314 entspricht. Wir wiederholten am übernächsten Tag noch einmal den Versuch, jedoch mit 1,5 ccm Zsp. Die Zsp. zeigte nun die Ger. Zeit von 8 Min. 30 Sek. während die Kontrolle erst nach 30 Minuten gerann, was einem Ger. Index von 361 entspricht. Wir gingen nun in den weiteren Versuchen in der gleichen Weise vor und konnten überall eine deutliche Ger. Aktivität der Zsp. und keine antithrombische Wirkung feststellen. Unsere neue Methode der abgekürzten Ger. Relation hatte sich also als sehr einfach und doch sehr empfindlich erwiesen. Vor allem konnte man erst jetzt der Frage nahe treten, welche Substanzen in der Zsp. es sind die diese Ger. beschleunigende Wirkung haben. Auf Grund unserer ersten Versuche hatten wir ja angenommen, dass es nicht unwahrscheinlich sei, dass in der Zsp. geringe Mengen von Thrombokinase und Prothrombin nebeneinander vorkommen. Wir hatten, worauf wir hier nicht noch einmal eingehen wollen das Vorkommen von Thrombin als Ursache der Ger. Aktivität der Zsp. ausgeschlossen. Aus dem Umstand, dass durch Aetherschüttelung die Ger. Aktivität der Zsp. herabgesetzt, durch Erhitzung auf 56° jedoch keine Beeinflussung der Ger. Fähigkeit auftritt hatten wir auf das Vorkommen von Thrombokinase geschlossen, die ja nach den Untersuchungen von *A. Schmidt* (19), *Morawitz* (15), *Howell* (11) und *Dyckerhoff* (7) in Aether löslich und thermostabil ist. Auf das Vorkommen von Thrombokinase haben wir auch auf Grund einer anderen Reihe von Versuchen geschlossen. Von diesen sei folgender erwähnt: schüttelt man Magnesiumsulfatplasma mit Aether, so dass es keine Thrombokinase mehr enthält, so kann mit Zsp. noch Ger. hervorgerufen werden, während die rekalkifizierte Kontrolle nicht gerinnt. Andererseits waren weitere Versuche nicht so deutlich zu klären. So konnte durch Erhitzung auf 56° bei ger. schwachen Zsp. eine Schwächung der Ger. Aktivität festgestellt werden, die eigentlich auf das Vorkommen von Prothrombin hindeuten würde. Doch wissen wir durch *Feissly* (8) u. v. a. dass es auch thermolabile Thrombokinase gibt. Andererseits würde der Kreuzversuch d. h. der Versuch durch lange Lagerung gealtertes Plasma durch Zsp. zureaktivieren, ein Versuch der sich leicht reproduzieren lässt, für das Vorkommen von Prothrombin sprechen. Besonders interessant nach dieser Richtung hin waren auch Versuche, in denen Zsp. nach *Bordet* (3) vorbehandelt worden waren, wobei die adsorbierten Proben eine längere Ger. Zeit aufwiesen als die nicht adsorbierten. Die an die Niederschläge des Calciumphosphats gebundenen Stoffe waren in Aether eluierbar, so dass man fast zur Annahme gezwungen wird, dass in der Zsp. die Thrombokinase nach *Bordet* eluierbar ist, da sich das Prothrombin in Aether ja nicht löst. Wir

haben als vorläufiges Kompromiss angenommen, dass sich Thrombokinase und Prothrombin, letzteres in geringer Menge oder in veränderter Form in der Zsp. befinden. Wir wissen ja auch von anderen biologischen Stoffen, dass es sich in der Zsp. unter anderen chemischen Bedingungen befinden. So können wir in jeder, auch der normalen Zsp., das Mittelstück des Komplements nachweisen, ohne dass sich der Eiweisskörper an den es im Blut immer gebunden ist in der Zsp. findet. Wir hatten auch daran gedacht, dass sich Teile der Ger. Faktoren in der Zsp. finden. So wäre denkbar, dass bloss eine Komponente des Prothrombins, z. Bsp. die Komponente A, in der Zsp. vorhanden ist. Oder aber es handelte sich um den von *Owren* (16) nachgewiesenen Faktor V. Dieser ist thermolabil und würde vielleicht die Ger. Abschwächung bei 56° erklären. Allen diesen Problemen werden wir mit unserer neuen Methodik nachgehen; in dieser Arbeit handelt es sich vor allem darum, mit einer relativ einfachen und einwandfreien Methodik mit *Sicherheit das Vorkommen ger. beschleunigender Stoffe in der Zsp. nachgewiesen zu haben.*

In Zusammenfassung unserer Ergebnisse kommen wir zu folgenden Schlussätzen:

- 1) In Fortsetzung früherer Studien konnte durch Verfeinerung der Technik es zur Evidenz bewiesen werden, dass die Zsp. Ger. beschleunigende Stoffe enthält.
- 2) Diese Technik bestand darin, dass die Zsp. in nativem Zustand, ferner citriert, dann citriert mit CaCl_2 -Zusatz auf Ger. untersucht wurde. Als Kontrolle diente das rekalkifizierte Plasma.
- 3) Es liess sich ein Index aufstellen, in dem die Ger. Zeit der Kontrolle mit 100 multipliziert und durch die Ger. Zeit. der citrierten und rekalkifizierten Zsp. dividiert wurde.
- 4) Die obengenannte Technik haben wir Ger. Relation genant. Eine abgekürzte Ger. Relation bestand darin, dass die Kontrolle um sie der Zsp. gleich zu setzen mit 0,02 ccm der 0,334 %igen CaCl_2 -Lösung versetzt und dann wie die Zsp. citriert wurde. Es erübrigte sich dann, das erste und zweite Röhrchen der Ger. Relation.
- 5) Auch bei der abgekürzten Ger. Relation wurde wie oben ein Index aufgestellt.
- 6) Mit Oxalatplasma ger. inaktive Zsp. von Paralyse- und Gehirnsyphilis wurden als *Hirschfeld-Klingersche* Reaktion gedeutet.

- 7) Eine Ger. inaktivität oder eine Zunahme der Ger. Zeit der Zsp. gegenüber der Kontrolle wurde in den meisten Fällen auf Veränderungen der pH zurückgeführt und konnte durch Ansäuern beseitigt werden.
- 8) Die endgültige Technik muss sich daher der abgekürzten Ger. Relation mit Bestimmung von pH und Angleichung der pH der Zsp. an jene der Kontrolle bedienen.

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A NEW KIND OF SENSE IN THE SKIN

By

ANDERS KRISTENSON

As is well-known, sensations of cold or heat, respectively, are caused if the cold and hot points are stimulated with suitable irritants. If these points are stimulated with hot objects, a painful, burning sensation arises, which is of the same nature on both kinds of points. A similar, possibly identical, sensation is elicited by a hot object from areas of the skin between the temperature points also, which appears to be due to stimulation of the painsense organ. It is possible that the quality of sensation from these latter places is not fully identical with the burning sensation from the temperature points, but has more the quality of pain.

If the tentacles with stinging organs of the so-called stinging jellyfish (*Cyanea capillata* Linné), met with on the west coast of Sweden during the summer, are allowed to affect the thin-skinned surface of a body, the following results will be noticed. The burning feeling is only elicited from the cold and hot points, and it is elicited practically immediately on contact between skin and tentacle. On skin areas without temperature perception no reaction is obtained until after some minutes, and then from surrounding temperature points. No effect can be proved on other kinds of sensibility qualities in the skin, especially on the pain sense.

The burning feeling from the temperature points may of course arise only owing to irritation by the toxin of the jellyfish. But what appears to be most characteristic is that the cold and hot points become hypersensitized, so that they react to extremely insignificant changes in temperature with an intense burning sensation, which is fairly immediate in its onset but somewhat protracted in duration. This hypersensibility persists for a long time (up to 24 hours or more) although it slowly abates. The perception of cold and heat is not appreciably influenced by the toxin of the jellyfish. The burning sensa-

tion can be elicited on the cold points, not only by means of slight cooling, but also by inappreciable heat stimulation. This applies also to the hot points, where not only heat but also slight cooling results in the burning sensation. It is not necessary to touch the skin with the hot or cold object, but it is sufficient to put the object close to the respective temperature points as long as a certain change in the temperature in the skin is effected. Even the cooling or warming of the skin which takes place if one blows on it leads to a reaction in the form of a burning feeling. Contact of the temperature points with objects which are indifferent in respect of temperature has no effect.

If a cold point is treated with chloroform for some minutes, it loses its capacity to react with a sensation of cold on being cooled. On the other hand, the reaction with a burning feeling to irritation with a hot object remains unchanged. Chloroform has the same effect on the cold point treated with jellyfish toxin as on the untreated cold point. It loses its capacity to perceive cold, but with an inappreciable change of temperature—heat or cold—an intense burning feeling arises. After some minutes the cold point gradually regains its capacity to perceive cold. Thus by means of a peripheral effect with chloroform a dissociated anesthesia can be obtained, in that the cold-perceiving organ is paralysed, but the capacity to react with a burning sensation persists.

By the application of a number of pharmaceutics from the adrenergic and cholinergic groups, I have endeavoured to elicit an effect similar to that of jellyfish toxin, but none of them, alone or in different combinations, gave positive results. Other pharmaceutics of various types have also been tried without result. With a carbolic-acid solution (1 %) the same effect on the cold points is obtained as with chloroform. With percaine both the temperature and burning sensations can be eliminated, but they cannot be differentiated from each other. Preliminary experiments with stinging nettles (*Urtica dioica* L.) have indicated that, in addition to another effect, an effect similar to that of jellyfish toxin presents itself. The hot points are not affected by chloroform or phenol in the concentration mentioned.

Thus, with jellyfish toxin the organ which transmits the burning sensation can be hypersensitized, and by means of chloroform and phenol the cold-perception can be eliminated, both in cold points affected by jellyfish toxin and in those unaffected by it. It was more difficult to effect an inhibition of the burning sensation at the same time as the cold perception was retained. By chance this was done successfully. In a couple of scars on the skin at the base of a septic infection I was able to prove the existence of a couple of cold points

within the scarred area. These cold points react normally to cold. On the other hand, they do not react at all to stimulation with hot objects which give rise to the usual painful burning sensation on the cold points outside the scarred area. Thus here a dissociated anesthesia had presented itself, in that only the cold perception persisted.

It seems to emerge from these observations that there is an organ in the temperature points and in the temperature-perceiving organ which reacts to hot objects with a burning feeling. The two organs are topographically-anatomically intimately connected with one another, but by means of different toxins and pharmaceuticals and other effects (jellyfish toxin, chloroform, phenol, septic processes) they can be dissociated from one another in functional respects. This probably cannot be satisfactorily explained except by the assumption that there is a special organ for the perception of heat which gives rise to the sensation of burning. This organ would then be equipped with special nerves and be represented by its own conduction paths and its own centres in the nervous system. Thus the assumption is arrived at that in the skin there is a kind of sense apart from those previously assumed: the senses of cold and heat, the sense of touch, the senses of pain and of pressure. This sense would serve to perceive heat, the burning sensation. In this connection it is of interest to point out that investigations during recent years have shown the existence of two kinds of nerve fibres in the cold points, which may indicate a double function of the organ of these points.

Are there any clinical experiences which indicate the existence of a special kind of sense for burning sensations? The question has probably been overlooked, in that the burning sensation has been confused with the pain sensations. It is well-known that in old people a burning sensation makes itself felt within certain areas of the skin, especially on the lower legs. Similarly, in the case of certain nerve diseases (*inter alia*, herpes zoster), a disturbance in feeling is met with, which consists more of burning smarting than of real pain. (Note the Danish name for herpes zoster, "Hell-fire".) To draw the border-line between these two sensations of pain and burning sensation is certainly difficult, but perhaps if attention is directed towards the conditions touched upon above, a differentiation may be possible.

SUMMARY

The cold and warm points appear to be associated with an organ for the perception of heat. This organ can be hypersensitized by the effect of toxin from the stinging jellyfish (*Cyanea capillata*). By the

influence of chloroform and phenol the cold sensation can be eliminated, but the sensation of heat persists in cold points whether treated with jellyfish toxin or not. In scars on the skin cold points may be met with which have no capacity to perceive heat. The existence of two different kinds of nerve fibres to the cold points may support the view that the latter have a double function. If there is a peripheral organ for the perception of heat, there should also be special peripheral nerves, conduction paths and central centres for that sense.

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ESTIMATION OF AMINES IN BLOOD FROM
SCHIZOPHRENIC PATIENTS AD MODUM
RICHTER, LEE, AND HILL, WITH DESCRIPTION
OF AN IMPROVED MODIFICATION
OF THE METHOD

By

IB MUNKVAD

During later years the intoxication problem in schizophrenia has occupied the attention of many biochemists. The first investigations of this problem (Weichbrodt, Baldi) apparently showed that serum from schizophrenics was more toxic than normal serum by intraperitoneal or intravenous injection in mice and rabbits. Later work by Wahlström and Sjövall has confirmed these results. Meyer states that he has found a positive Congo red test in 60 schizophrenic patients, which is an indication that the reticuloendothelial system has been blocked. This author regards his findings as evidence in support of the intoxication theory. Meyrat has found increased xanthoprotein values in a large number of schizophrenic patients, especially catatonics. However, the results of Meyer and Meyrat have not been confirmed by later workers.

We further mention the work of Gjessing on the phasic N-retention in periodical catatonies and his hypothesis that in schizophrenia we are confronted with the action of rather high-molecular products, especially toxic amines, arising from the breakdown of proteins. The investigations of Gjessing led Richter, Lee, and Hill to take up the problem and work out a new method for the determination of amines in blood. However, on application of their new method, they did not find any amines at all in the blood of 58 selected psychotic patients of different types, while they actually observed a slight increase of the amine-lipoid fraction in 18 schizophrenics. Furthermore these authors criticise Gjessing's intoxication theory, inasmuch as they maintain that several N-containing breakdown products are comprised by the retention and not only a single compound. They also assert that the fundamental disturbance is not to be found in a single inter-

TABLE 1

The efficiency of extraction for various solvents with respect to an aqueous amine solution.

Solvent	Extinction coefficient	Wave gauge
Benzene	130	410
Xylene	20	450
Toluene	64	420
Rect. gasoline	42	410
Ord. gasoline	68	410
Kerosene	72	430

mediary link, which might possibly be the cause of the presence of toxic amines in the blood, but that the disturbance comprises the whole protein metabolism.

The purpose of the present investigation has been to develop a more sensitive method than the one described by Richter, Lee, and Hill, since that method suffers a. o. from the drawback, already pointed out above, that it did not permit the demonstration of the presence of amines in the blood of normal subjects or in that of schizophrenics. Amines such as β -phenyl-ethyl-amine, or the higher aliphatic amines produced by putrefactive bacteria, are most suitable for estimation by this method.

The method of Richter et al. consists essentially in the extraction of the amines from blood samples by shaking with light petroleum and excess of normal potassium carbonate. Beforehand a small amount of tyramine hydrochloride is added to the blood in order to prevent a loss of amines through the formation of Schiff's bases, since amines combine with traces of aldehydes. The amines are separated from the phospho-lipoids by being shaken over into a small volume of 1 n sulphuric acid saturated with sodium bromide. By this procedure the phospho-lipids remain in the petroleum. The amines are then trans-

TABLE 2

Addition of isobutyl amine to 10 ml normal blood (the same blood sample is used throughout).

Isobutyl amine	0 γ	10 γ	25 γ
Extinction coefficient	52	89	140
Corrected extinction coefficient	—	+ 37	+ 88

TABLE 3

Content of amines in the blood of 10 normal subjects.

Subject	Age	Sex	Extinction coefficient
E.O.	35	♂	82
S.W.	43	♂	37
K.M.S.	48	♂	51
S.P.	36	♂	34
K.M.	30	♂	54
T.A.	36	♂	64
E.N.P.	33	♂	44
H.N.	37	♂	20
M.S.	36	♀	51
M.M.	46	♀	43

Average value of ext. coeff.: 48, corresp. to 13 γ isobutyl amine or 1.3 γ per ml.

ferred to light petroleum again by shaking, and picric acid is added. The picrates formed show a strong yellow colour in chloroform.

To begin with this method was applied to the blood of 10 schizophrenic patients chosen at random, but the presence of amines could not be demonstrated.

Proceeding now to a more accurate analysis of the method of Richter et al. our attention was drawn to the nature of the shaking medium, specified as light petroleum with a boiling point of 80-100°. In the initial experiments rectified gasoline had been employed on account of its presumed similarity to light petroleum. Suspecting that the shaking medium was inefficient, we examined various types of solvents. This was done by adding 3 ml solvent and 0.2 ml 40 per cent potassium hydroxide to 1 ml aqueous amine solution, containing 5 γ isobutyl amine per ml. This mixture was shaken for 6 minutes and then centrifuged. The shaking medium was now removed and 3 ml chloroform and 0.1 ml 2 per cent picric acid in chloroform were added to it. At the same time a blank was prepared in exactly the same way as just described, but with 1 ml distilled water instead of the amine solution. The colorimetric measurements were carried out with Coleman's photocell colorimeter. The wave gauge giving maximum extinction was employed. The results are given in Table 1.

In accordance with these results benzene is used as shaking medium. Furthermore we have added isobutylamine (10 γ -25 γ) to 10 ml normal blood. The extinction-coefficients with benzene as shaking medium are given in table 2. The further details of the method are as follows.

TABLE 4

Content of amines in the blood of 20 schizophrenic male subjects.

Date	Name	Journ. no.	Diagnosis	Extinction coefficient
27/5	E.S.	10675	schiz. cat.	60
27/5	C.P.	8972	hebephrenia	51
27/5	A.J.	11588	schiz. cat.	62
27/5	A.B.A.	8749	"	71
29/5	H.F.T.	11656	"	60
29/5	H.J.R.	7794	"	65
29/5	G.A.C.	8497	"	48
29/5	G.C.N.	9755	"	69
1/6	K.R.	15231	catatone stupor	55
1/6	W.S.	14151	"	50
1/6	L.A.	14422	schiz. cat.	64
3/6	Th.H.	9041	"	48
3/6	E.B.G.	10381	"	48
4/6	A.R.C.	6218	"	60
4/6	J.C.	9701	"	52
4/6	E.K.N.	8361	"	78
4/6	H.H.	9833	"	85
28/6	G.R.	15218	"	35
28/6	P.S.	15146	"	62
28/6	R.F.	9477	"	52

Average value of ext. coeff.: 59 corresp. to 16 γ isobutyl amine or 1.6 γ per ml.

10 ml oxalate blood are transferred to a 30 ml centrifuge tube, where 5 mg tyramine hydrochloride in substance are added under stirring. 10 ml benzene and 5 ml saturated potassium carbonate are then added, and the mixture is vigorously shaken for 3 minutes. After centrifugation 7 ml of the benzene layer are transferred to a 10 ml centrifuge tube containing 0.5 ml 1 n sulphuric acid saturated with sodium bromide. After shaking for 4 minutes the mixture is centrifuged and the benzene layer removed. The acid solution is washed with 3 ml benzene by shaking for 3 minutes, and centrifuged again, whereupon the benzene layer is removed once more. The amines are now brought back into benzene solution again by adding 3 ml benzene and 0.2 ml 40 per cent potassium hydroxide and shaking for 6 minutes. After centrifuging the benzene layer is transferred to a clean, dry tube, and 3 ml chloroform and 0.1 ml 2 per cent picric acid in chloroform are added. The photometrical measurements are carried out as described above. A blank is prepared from 10 ml distilled water instead of blood.

TABLE 5

Content of amines in the blood of 20 schizophrenic, female subjects.

Date	Name	Journ. no.	Diagnosis	Extinction coefficient
14/6	T.A.	224	schiz. cat.	28
14/6	A.R.	243	"	27
14/6	R.W.	335	"	32
14/6	C.S.	249	"	68
16/6	J.E.J.	34	"	37
16/6	B.F.	5	"	25
16/6	L.A.	448	"	90
16/6	M.R.	97	"	10
18/6	H.N.	20	"	38
18/6	A.C.	284	"	35
18/6	J.F.C.	3	"	33
18/6	E.J.	18	"	45
21/6	L.S.	27	"	68
21/6	C.R.	152	"	51
21/6	G.P.	314	"	80
22/6	R.J.	191	"	22
22/6	E.L.	205	"	45
22/6	E.J.	18	"	42
8/7	M.C.N.	331	"	44
8/7	A.E.	372	"	42

Average value of ext. coeff.: 43 corresp. to 12 γ isobutyl amine or 1.2 γ per ml.

This method was now applied to the estimation of the amine content in the blood of 10 normal subjects together with 40 schizophrenics, 20 males and 20 females. The material mainly consists of catatonic forms of schizophrenia. The female subjects have been patients at the hospital for many years. In the male material we have included, together with the older cases, 5 patients whose illness must be characterised as being in an initial stage. (Journal nos. 15231, 14151, 14422, 15218, 15146). The results are given in Tables 3, 4, 5.

It will be seen that the average value of the content of amines in the blood of schizophrenic females (Table 5) is slightly lower than the corresponding value for males (Table 4). The difference is, however, too small to be significant. Furthermore, there are larger deviations from the average value in the female than in the male material. The value found for the content of amines in the blood of normal subjects (Table 3) is practically equal to the mean of the average values for schizophrenic males and females. Thus, by the more sensitive method here described it has been impossible to find increased values for the

content of amines in the blood of schizophrenic patients. Due regard must be paid to the smallness of the material, but there does not seem to be any difference between the content of amines in the blood of older and younger catatonic forms of schizophrenia (Table 4).

SUMMARY

(1) A more sensitive modification of the method of Richter, Lee, and Hill for the estimation of amines in the blood is described. As little as $\frac{1}{2}$ γ isobutyl amine per ml blood can be detected, when 10 ml blood are used.

(2) The content of amines in normal blood, when expressed as isobutyl amine, is found to be 1.3 γ per ml.

(3) Increased values for blood amines could not be detected in 40 schizophrenic patients, mainly catatonic forms with distinct physic alterations.

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EXPERIMENTAL CATATONIA

By

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Disturbances of muscle tonus and movement are fairly common symptoms of pathological conditions affecting the central nervous system. In most of such cases there is generalized or extensive tissue damage. However, even relatively circumscribed lesions can give rise to pronounced and severe symptoms of this kind. This is also true of *catatonia*. In catatonia there is increased muscle tonus with plastic rigidity of the musculature, a *flexibilitas cerea*; voluntary mobility is reduced and the individual is therefore able to maintain postures, whether spontaneously adopted or induced, for longer or shorter periods. Apart from all sorts of generalized brain lesions, catatonia may be caused by pathological processes limited to the central parts of the brain stem, e.g. in cases of lethargic encephalitis. *Von Economo* has expressed the opinion that an inflammatory process in the periventricular grey matter at the junction between the third ventricle and the Sylvian aqueduct is the lesion responsible for the occurrence of catatonia. In lethargic encephalitis it is not uncommon to meet with *catalepsy*, i.e. the simultaneous occurrence of catatonia and sleep. Catatonia is also known to occur in schizophrenia, but in this case the lesion responsible is unknown.

It has been known for quite a long time that certain drugs can cause a catatonic condition in experimental animals (cf. *de Jong & Baruk*). Bulbocapnin has been the drug most used in experimental work. The fact that catatonia cannot be induced with this drug in animals lacking a neo-cortex has been taken to indicate that in higher animals the cortex is somehow involved in the causation of catatonia. According to *de Jong & Baruk* not only exogenous intoxication can produce catatonia, but endogenous intoxication may do so, too. These authors believe that a disturbance of liver function is common to all these intoxications. They therefore consider that liver damage is of

primary and decisive significance in the production of catatonia. Against this view go results of experiments showing that small injuries within the vegetative centres of the brain stem may lead to catatonia.

The first to evoke catatonia in experimental animals by means of small injuries to the brain stem seems to have been *Demole*. In connection with his work on the hypnotic effects of Ca and K salts when injected into the region of the hypothalamus he incidentally observed catatonic muscular rigidity in the experimental animal. However, his expectation that experimental studies of the hypothalamus would shed light on the problem of catatonia has only been partly justified. The literature contains but little information on the subject. The only large series of experiments to be found in the literature was described by *Ingram, Barrie & Ranson*. These authors obtained catalepsy in 55 cats after electrolytic necrotisation within the posterior part of the hypothalamus. When the catatonia was at its highest the animals could be placed in the most peculiar positions and would maintain them for longer or shorter periods. The muscles showed the characteristic plastic rigidity. The sleep which formed part of the cataleptic syndrome only lasted a few days while the catatonia showed considerable variation in its duration, lasting from a few days to 10 months, i.e. throughout the whole period of observation. In some cases it may therefore be considered a permanent symptom.

In considering the localisation of the damage giving rise to catalepsy, *Ingram et al.* maintain that it requires a widespread bilateral destruction of the tissue lying between the mamillary bodies and the red nuclei. This view is in agreement with the opinions expressed by von Economo.

During attempts to induce sleep experimentally in cats by bilateral electrolysis within the posterior parts of the hypothalamus the present author has also observed on some occasions the occurrence of catatonia simultaneously with the sleep effect.

The electrolytic necroses were placed in the positions described by the use of the *X-ray stereotactic instrument* which has been described in detail in an earlier publication (*Ranström 1947*). All the operations were performed under nitrous oxide anaesthesia.

RESULTS

Cat 22. Operation 24/5/35. Electrolysis from 15.20 to 15.25. Operation completed 15.30.

The animal wakened after a bare 5 minutes, walked around in its cage and moved in an apparently completely normal way. After an hour or so it gradually

became stiffer in its movements. At about 17.00 it was markedly catatonic and definitely sleepy. It had spontaneously taken up a position with its back arched and its head bent downwards between its forepaws (fig. 1). It remained in this position for hours on end. No nystagmus could be observed. Every now and then it changed its position by means of very slow stiff movements. Sometimes it lay on its side and slept, but even then the muscles were very stiff and showed the typical wax-like rigidity. From time to time it spontaneously took up the position described above, with the head bent down and the back arched. Even when it stood in this position it was apparently asleep. The condition remained substantially unchanged for more than 48 hours (fig. 2). During 27/5/47 the animal woke up,



Fig. 1.
Cat 22, 24/5/45.



Fig. 2.
Cat 22, 25/5/45.



Fig. 3.
Brain stem of Cat 22.

but the catatonia persisted. During the following week the catatonia gradually disappeared and by 3/6/47 the animal moved with its usual ease, and no more muscular rigidity could be observed.

The later course of the condition was characterised by markedly stereotyped movements; the condition became apparent about 1 month after the operation. The animal practically never lay still in the cage as it used to do before the operation. It nearly always stood in the same position in the same place in the cage. It stood with the left forepaw raised and incessantly repeated the one movement of stamping cautiously with that paw, for the most part, however, without touching the ground. Its appetite and thirst appeared unchanged. The animal did not become fatter or thinner. The condition remained stationary during the whole period of observation. At almost every observation the animal was found to be standing in the same position and carrying out the same stamping movements with the left forepaw. It took but little notice of its surroundings and seldom moved away when the observer tried to touch it, and never became enraged like ordinary stray

cats do, and as it used to do itself before the operation. The animal was under observation for 20 months and was then killed.

The autopsy showed no macroscopic findings worthy of note.

Microscopy showed glial scars in the brain stem. Their extent is shown in the schematic sketch in fig. 3. Nothing of interest was found in such of the other organs as were examined.

Cat 25. Operation 13/6/45. Electrolysis from 13.35 to 13.40, operation completed 13.45.

After 6-7 minutes the cat was wide awake again, but it was noticeably stiff in its movements. After another half hour marked catatonic muscular rigidity was observed, the whole body being stiff, including the tail. It reached quickly however, if disturbed. By 16.00 it had adopted a position with its head bent downwards and forwards and the back arched. If it was laid on its side it got up at once, or after a short interval, and again took up the same position. This was done

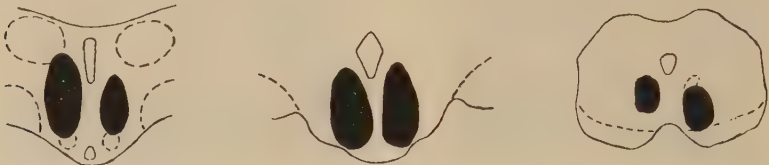


Fig. 4.
Brain stem of Cat 25.

with very stiff movements. Sometimes it lay down and became extremely somnolent, and slept intermittently. It remained somnolent during those longer or shorter periods when it was standing in the catatonic arched position. Its condition remained unchanged throughout that day (the last observation was made at midnight). By the morning of 14/6/45 the catatonia had completely disappeared and the animal lay in a peaceful sleep with its muscles relaxed, it was quite easy to wake it. It remained in the same peaceful sleep during the next two days and even on the morning of the third (17/6/45). It then received a subcutaneous injection of 20 ml. of physiological saline. After this it rapidly awakened. It then walked about freely, without any stiffness of its movements.

During the later course of the condition the animal showed slowly progressive and extreme emaciation, which occurred in spite of a definite increase in the appetite. If it was allowed to do so it would eat everything that was set before it till, finally, it was sick. It would then quickly eat up its vomit. No increased thirst was noticeable. The most striking symptom, however, was the occurrence of epileptic attacks of the classic type, with a tonic contraction for a few seconds; this was followed at once by clonic contractions of such violence that the animal was thrown forwards and backwards between the walls of the cage. After this there was a short period during which it lay still with its muscles relaxed and did not react when moved. The whole attack lasted 1 or 2 minutes. The animal got up immediately after the attack and moved about in a more or less normal way. It seemed, however, to be in a state of constant restlessness and never lay still in the cage but walked about, usually backwards and forwards. The first attack was observed about 3 months after the operation. It was hard to estimate the frequency of the attacks. One or two attacks were generally observed to occur dur-

ing the daytime in each week and attacks were also observed to occur during the night. The animal died 11 months after the operation. Death was thought to have occurred during an attack.

Post mortem examination showed extreme emaciation, but nothing else of interest.

The microscopical examination of the brain stem showed glial scars over the area shown in fig. 4. There was no demonstrable tissue damage or scars in the regions through which the electrodes were inserted. There were no obvious histological changes in the hypophysis.

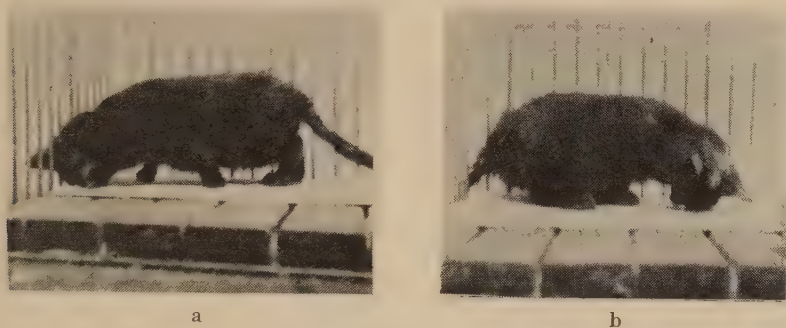


Fig. 5.

Cat 31, 15/10/45; a, in the morning; b, in the afternoon.



Fig. 6.

Brain stem of Cat 31.

Cat 31. Operation 14/10/45. Electrolysis from 13.50 to 13.55, operation completed 14.00.

The animal wakened after 2 minutes, and walked around in the cage. After a further 5 minutes it lay down and remained lying down most of the time for the rest of the day, only getting up occasionally during the afternoon. Late that evening it was observed that its movements were remarkably slow and stiff, if it was made to walk about the cage. On the morning of 15/10/45 the animal was noticeably sleepy, it stood for long periods with its head bent downwards and forwards but with its back straight (see fig. 5). During the afternoon it lay asleep off and on when it was not disturbed. The waxlike rigidity remained unchanged during the whole of that day. The animal remained in a peaceful sleep during the whole of 16/10/45, but its muscles were still definitely rigid. On 17/10/45 the animal was still somnolent, but did not sleep for long stretches on end. It was very angry if disturbed. The muscular rigidity had almost disappeared. On 18/10/45 the cat was in much better form and showed no more catatonia. It still showed no noticeable abnormality of behaviour or muscle tonus on 19/10/45. On the morning of

25/10/45 it was found dead in its cage and post mortem examination showed no cause of death outside the brain (no bronchopneumonia, meningitis, or intracranial haemorrhage).

Microscopical examination showed areas of fresh necrosis in the brain stem as shown in fig. 6.

Cat 41. Operation 4/3/46. Electrolysis from 13.40 to 13.45. Operation completed 13.50.

The animal awakened immediately. At about 15.30 it began to be listless and



Fig. 7.
Cat 41, 4/3/46.



Fig. 8.
Cat 41, 6/3/46.



Fig. 9.
Brain stem of Cat 41.

after some time it got more and more somnolent and tended to sleep when not disturbed. Immediately after 16.30 it was sleeping peacefully, but a little later it got up and took up the "ordinary" catatonic arched position, though its head was not between its forepaws but to the left of them (fig. 7). The characteristic wax-like muscular rigidity was present. The animal seemed to sleep properly even in this position. It could, however, be awakened. Now and then it lay down, but even then its muscles were stiff. Its condition remained the same throughout that night, sometimes it lay down and sometimes it stood in the arched position, but it was asleep all the time. It slept for the whole day on 5/3/46, mostly lying down, sometimes standing for a short while in the arched position. The condition was still the same the next day, the catatonic rigidity was still present (fig. 8), also when the animal was lying down. On the following day (7/3/46) the cat awakened, it was perhaps slightly listless, but scarcely enough so to be considered somnolent. It moved stiffly when made to move about in the cage, but otherwise it lay still for the most part. On a few occasions during the day it took up the

arched position, but never held it for more than half a minute at the most. By 8/3/46 the stiffness was gone. The animal spent most of its time walking about in the cage and seldom lay down. This cat, which was very fierce before the operation, had become far more good-natured. One could pat it without it trying to turn on one, which would have been impossible before the operation. When it was observed the cat was always found to be walking slowly backwards and forwards in the cage. The condition remained unchanged till 18/4/46, when the animal was killed.

Microscopical examination showed areas of necrosis in the brain stem as shown in fig. 9.

DISCUSSION

The results of the present experiments agree well with those of *Ingram et al.* as to the site of the lesions causing catatonia. The lesions included the area between the mamillary bodies and the red nuclei. It is impossible, as yet, to draw any conclusions as to why catatonia only occurred in a few of the experiments, in all of which the lesion was substantially in the same area. This fact makes it very hard to localise exactly the part of the brain stem which must be destroyed if catatonia is to ensue.

The catatonia was typical, with wax-like rigidity, a decrease in spontaneous movements, and ability to maintain the body in one position for long periods. This is also in agreement with the findings of *Ingram et al.* The present experiments were more concerned with the sleep-producing effect of the lesions than with alterations in muscular tonus; so the animals were mostly left in peace. They were only disturbed for observations at regular intervals of the depth of the sleep; the muscular tonus was observed at the same time. No attempts were therefore made to find out to what extent the animals could hold passively induced positions. On the other hand this provided the opportunity of observing how *the animal took up certain positions spontaneously, and how it sometimes, also spontaneously, returned to the same position when it had been made to give it up.* The most striking position, which was seen in all 4 experiments, was that in which the head was bent downwards and forwards with or without arching of the back. It is naturally very hard to give an interpretation in terms of disordered function, of this perseveration of a position which has been adopted spontaneously.

In one of the present experiments the catatonia came on immediately after the operation, in the rest its onset was delayed for one or more hours. However, the effect was found to increase markedly during the first 24 hours after the operation as to the time of onset

of the catatonia. The way in which the catatonia increases after the operation would appear to suggest that it is not only the actual areas destroyed which are involved in the mechanism causing this condition, but that the effect of the necroses on the surrounding parts of the brain also plays a part. For the present, however, it is impossible to form any opinion as to the nature of this effect. In three of the four experiments described here the catatonia passed off gradually (in the fourth it disappeared in the course of one night during which no observations were made; it is therefore impossible to say whether it passed off suddenly or gradually). It is clear that the catatonia disappeared slowly in the cases of *Ingram et al.*, too.

The abnormalities seen in the later stages of the condition, after the sleep and catatonia had both gone, are of interest. They consist of *stereotyped movements*, *epilepsy*, and *excessive appetite*.

The stereotyped movements seen in Cat 22 are remarkable, they lasted nearly 2 years until the animal was killed. The mechanism underlying this abnormality is also unknown. The only state in which a similar condition occurs in man would appear to be schizophrenia.

It is, of course, possible that the epilepsy seen in Cat 25 was caused by cortical damage at the site of insertion of the electrodes, even though no such damage could be demonstrated at the microscopical examination, and although the fits were not of a Jacksonian type. The combination of epilepsy and excessive appetite was particularly noteworthy as such a combination of symptoms is not unusual in man. In fact such excessive appetite is seen in association with a large number of extensive lesions of the brain, especially those affecting the frontal lobe. It is, however, known that artificial lesions confined to the hypothalamus can give rise to this symptom. *Brügger* and *Brobeck et al.* have previously described similar experimental results. The experiments of *Brobeck et al.* were performed on rats. The animals put on weight, a result which was ascribed by the authors to the excessive appetite and not to any disorder of metabolism. In Cat 25, however, the increase in appetite was associated with a marked loss of weight, which suggests that there was really a metabolic disturbance. Such disturbances are commonly associated with lesions of the hypothalamus in man.

The derangements described above, occurring as late sequelae to electrolytic necrotisation within the posterior part of the hypothalamus, have not been observed in a single other case although nearly 50 such experiments have been performed. It is as yet too early to discuss whether or not these disorders stand in any causal relationship with the occurrence of catatonia in the immediate postoperative period.

SUMMARY

Catatonic rigidity lasting one or several days was observed in 4 experiments on cats in which electrolytic necrotisation was carried out within the posterior part of the hypothalamus. No explanation is advanced of the fact that in the great majority of the experiments in which the lesions were in a similar situation within the brain stem no catatonia occurred.

Stereotyped movements were observed as a late sequela in one of these cases. They persisted for a long time. In another case epilepsy of the classic type was observed in association with excessive appetite and extreme emaciation.

The pathophysiology and exact anatomical basis of all these late symptoms are obscure.

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SYNDROME SCHIZOPHRENIQUE JUVENILE ET MACROMASTIE

Etude clinico-psychologique.

Par

M. SCHACHTER

L'observation que nous nous proposons de relater, présente à notre sens son intérêt non seulement du fait de l'exploration au test psychodiagnostique (Rorschach) que nous avons pu pratiquer, mais aussi et surtout à cause de l'existence, chez cette malade, d'une macromastie remarquable que nous n'avons jamais encore rencontrée, sous cette forme, à 17 ans, ni encore moins chez un sujet présentant un syndrome mental net.

Obs. S. L. âgée de 17 ans 2 mois, nous est amenée par sa mère, pour des troubles dans le comportement. « Elle n'est pas comme tout le monde » dit cette femme simple, pendant que sa fille se tient à côté d'elle et semble ne pas s'intéresser ni à nous, ni à nos assistantes qui la regardent.

S. L. est le 3-e enfant ; les deux qui l'ont précédée, sont morts, l'un à 12 mois d'une diphtérie ; l'autre à 14 ans, d'une péritonite. Après elle, se situe une fausse couche aux environs de 7 mois et un enfant, actuellement âgé de 9 ans, qui—selon la mère—serait en bonne santé physique et mentale.

Le père, décédé à 43 ans, était un alcoolique, tabagique et « fort nerveux » ; il était le *cousin germain* de sa femme. Donc, notre patiente est la descendante de *parents consanguins*. Il n'y aurait pas de cas de maladies mentales dans la fratrie de notre malade.

La grossesse était normale et l'accouchement eut lieu à terme, mais l'enfant cyanosée à dû être ranimée ; elle pesait 3300 gr. et fut mise au sein pendant 3 mois.

Le premier développement (dentition, marche et parole) fut normal. En ce qui concerne le contrôle sphinctérien, S. L. a été énurétique jusqu'à l'âge de *douze ans*. Depuis cette date, elles urinait, de temps en temps la nuit ; enfin, au cours des derniers 3-4 mois, elle mouille *de nouveau*, le lit presque régulièrement ; la nuit seulement.

Comme antécédents pathologiques, nous notons une rougeole et une varicelle vers 24 mois ; une coqueluche, non compliquée, vers 30 mois.

Scolarité : est allée en classe jusque vers 11 ans, quand elle fut envoyée, pour suspicion de tuberculose pulmonaire (non confirmée) dans un préventorium.

Jamais de certificat d'études primaires. Sait lire et écrire très convenablement, ainsi que nous avons pu le constater.

Maladie actuelle : au cours de l'année 1947, étant-avec sa mère- dans une colonie de vacances (sa mère y était comme serveuse), à la suite de mauvais traitements (?) ou d'une peur (?), S. L. a commencé à devenir agitée, à parler seule (c'est à dire à marmoter des mots que l'on ne comprenait pas), à faire des gestes absurdes (gesticulations, clignements des paupières, grimaces, en sortant la langue et en la bougeant dans tous les sens), à ne plus se laver, devenant sale et négligée (pour une fillette de 15 ans, cela ne pouvait pas passer inaperçu). De plus, on a constaté que son comportement changeait sans cesse : tantôt elle se montrait sérieuse, obéissante, comprenant les ordres qu'on lui donnait; tantôt, au contraire, elle était puérile, souriant bêtement, se montrant indifférente aux stimuli de l'ambiance ou se mettant en colère pour la moindre des choses.

Ces derniers traits caractériels et de comportement, nous pouvons les confirmer pleinement. Elle n'est pas capable, actuellement, de faire la moindre commission, car elle oublie ou ne fait pas du tout attention à ce qu'on lui dit; et pourtant, elle comprend parfaitement bien de quoi il s'agit. Mais, on a l'impression que nos paroles ou ordres *glissent* sur elle, sans la toucher. Elle est *maniérée*, ses grimâces changent, pour ainsi dire, tout le temps. A nos questions, nous avons tantôt des réponses laconiques, stéréotypées : « je sais pas », « non », « oui », tantôt au contraire, elle devient loquace et alors elle s'exprime de façon remarquablement stylée, utilisant même des expressions littéraires et scientifiques, tout cela *de façon impeccable*.

Lui demandant si les médecins de la colonie de vacances l'ont soumis à un traitement quelconque, elle devient brusquement sérieuse et taciturne; après quelques instants : « croyez-vous que ces *petits médecins* comprennent quelque chose à ces affaires psychologiques; ils croient que je suis folle mais alors, docteur, dites-moi, si une folle sait raisonner comme je le fais; si une folle sait juger la bêtise de ces gens qui se croient si instruits ». Tout ceci est dit avec une allure sérieuse, tout en nous regardant directement en face.

Entendant parler de débilité mentale, elle dit : « un débile mental ne sait pas parler, ne comprend pas ce que vous lui dites; alors, moi qui comprend tout ce que vous dites, je ne suis pas une débile mentale ».

Ces quelques traits, venant corroborer les dires de la mère de cette jeune fille, situent immédiatement le diagnostic de syndrome schizophrénique, indubitable.

A l'examen *somatique* nous notons : une constitution pycnique plutôt; taille 145.5 cm (au lieu de 155), poids : 45 (au lieu de 47); tête fine, petite, des traits du visage très délicatement dessinés. Squelette normal par ailleurs. Or, la déshabillant un peu, nous sommes frappés par le *volume énorme des glandes mammaires*, qui descendent pratiquement jusque vers l'ombilic. Il s'agit de *seins normaux*, dont la grandeur rappelle bien celle d'une femme adulte, gestante; le pannicule glandulaire se palpe facilement; l'aréole est bien pigmentée, le mamelon de type adulte; on note des tubercules de Montgomméry bien figurés. La palpation des seins n'est pas douloureuse : aucun symptôme pathologique.

Sphère sexuelle : pilosité axillo-pubienne très bien développées. Les règles sont régulières, durent 4-5 jours et sont indolores. Aucune expérience sexuelle.

Les autres viscères sont normaux; thyroïde nettement palpable, mais non augmentée de volume. Système nerveux : réflexes normaux et égaux. Rien au point de vue des réflexes oculo-pupillaires. Pas de troubles trophiques.

Le test de *Rorschach* est accepté sans résistance. Nous reproduisons textuellement le protocole, seulement pour souligner le langage utilisé par la malade :

- I. « Un papillon » (toute la planche : GF + An V) ; « ah, c'est des tests : quand j'étais dans la maison des fous on faisait ça ; il y avait des idiots que le Dr. S. étudiait tout le temps ». (Grimâces et rires).
- II. « Deux petites filles » (« bonnets » rouges, haut : DK H O) ; « il faut voir encore autre chose ? non, plus rien ». (retourne la planche deux fois).
- III. « Ca c'est un lion » (haut rouge : DF + An) ; « des animaux, oui, des singes ; non, je ne crois pas ; c'est des chiens » (noir, « Messieurs » : DF + An).
- IV. (retourne 3 fois la planche) : « oh, ça, je ne sais pas ; à quoi ça ressemble ? c'est peut être ... *c'est une ressemblance à rien du tout* » (Réfl. abstr.).
- V. (retourne 2 fois) : « un papillon, non, oui » (GF + An V).
- VI. (retourne 2 fois) : « ça aussi un papillon ; ce n'est pas vrai ! *je dis n'importe quoi ; je ne me tracasse pas la tête ; quand je ne sais pas, je dis que je ne sais pas !* » (donc, DF + An, haut ; ensuite refl. abstr.).
- VII. (retourne 2 fois) : « deux figures qui se regardent » (DK H V).
- VIII. « deux lions ou tigres » (DF + An V), « un sapin » (haut centre : DF + Bot), « *si ce n'est pas ça, eh bien ça ne fait rien, non plus* » ! (refl. abstr.).
- IX. (retourne 4 fois) : « deux physiognomies » (haut, « mages » : DF + H), « je ne sais plus rien ».
- X. (retourne 3 fois) : « un cerf » (brun lat : DF + An) ; « je ne sais pas si les autres sont des animaux ».

Remarques : L'examen structural du protocole donné par la malade, nous montre les faits suivants : Nombre des réponses interprétables : 11.

G-2 ; D-11 ; F+ 8 ; F+ 1 ; F+ 1, F+% 88 ; K-2 ; chromesth. : O ; soit 2/0, introversivité : An% = 54 ; H% = 36 ; Bot. 9%. Vulg. 36% ; Orig. 9%.

En somme, nous retenons le type de perception qui est abstrait, synthétique, un peu raide et même prétentieux ; mais en tout cas, les interprétations sont valables. L'intelligence exprimée en F+ est bonne ; le type de réaction (« Erlebnisstypus ») est introversif, de façon nette. Absence de toute interprétation chromesthésique, dénotant, symboliquement, cette véritable anesthésie affective qui caractérise l'état mental de la malade. Aucun élément autosomatique (c'est à dire absence d'interprétations *Anat.*). La capacité de discerner et de comprendre, intellectuellement, l'ambiance, symbolisée dans le pourcentage H, est optima ; peut-être même trop accentuée, dénotant un penchant *pathologique* à « couper les cheveux en quatre ». Effectivement, parfois, la malade donne l'impression d'être attentive à des choses qui échappent à un observateur normal.

Mais, contrastant avec ces *données objectives* du test, nous avons vu, plus haut, la relative fréquence des remarques abstraites, si fréquentes dans les états mentaux caractérisés. Ajoutons aussi, la réflexion abstraite typiquement schizoïde, à la pl. IV qui est ensuite *refusée*.

En somme, l'incohérence mentale de la malade saute aux yeux également dans le test de Rorschach, où les réponses correctes, « bien vues » voisinent ou alternent avec des remarques abstraites.

Si nous résumons, maintenant, notre observation, nous constatons chez cette jeune fille un ensemble symptomatique qui est hautement évocateur d'un état schizophrénique. Effectivement, nous y retrouvons la plupart des traits cliniques considérés comme typiques. On sait, que chez ces malades on peut noter : des troubles dans les rapports avec l'ambiance (tendance à l'isolement, régression de l'intérêt à s'attacher au milieu) ; troubles de la parole (mutisme ou au contraire, logorrhée, bégaiement, néologismes, phonographisme, changement continu du ton de la parole), troubles affectifs (anxiété, irritabilité, dissociation affective, régression affective, indifférence ou anesthésie affective) ; troubles de la vie instinctive (apathie, irritabilité, crises imotivées de colère, fugues, grimâces, ricanements absurdes) ; troubles de l'association (idées bizarres, incohérentes, négativisme) ; catatonie (rare chez le petit enfant) ; troubles généraux divers (par ex. énurésie, après une période de propreté, comme chez notre malade) : mouvements rythmiques lors de l'endormissement (*jactatio capitis*), onanisme, gâtisme.

L'examen psychologique au test de Rorschach, nous a montré, encore une fois, cette même incohérence ; à côté d'interprétations de qualité incontestable, des remarques déplacées (voir réponses aux pl. I, III, IV, VI, VIII).

Enfin, du point de vue somatique, nous avons insisté sur l'existence d'une *macromastie bilatérale* très importante, non douloureuse, c'est à dire que l'on ne peut pas considérer comme étant le siège d'un processus pathologique. Les stigmates sexuels de la malade sont normaux et sa formule menstruelle pratiquement normale.

Nous avons cherché dans la littérature la question de la morphologie des glandes mammaires chez les malades mentaux. C'est seulement parmi les travaux de l'école endocrinologique roumaine (prof. C. I. Parhon) que nous avons trouvé des données sur ce thème particulier. Ainsi, C. Parhon-Stefanescu, étudiant (1930) ces glandes chez 100 malades d'asiles, a trouvé 6 fois (soit 6 %) des hypertrophies mammaires incontestables. Il s'agissait de 2 cas de schizophrénie ; 1 cas de paranoïa ; deux oligophrénies et une PG. Cet auteur cite, par ailleurs, une observation de C. I. Parhon, Urechia et Popea, concernant une association d'idiotie et de macromastie. Toujours en Roumanie, P. Radu et A. Blinov (1930) ont publié l'observation d'une idiote microcéphale avec hypermastie bilatérale ; enfin, une nouvelle observation de nanisme hypophysaire avec macromastie et oligophrénie a été relatée par C. Parhon-Stefanescu, A. Blinov et I. Ornstein (1937).

Il n'est pas dans notre intention de discuter les corrélations qui unissent cette véritable paramorphose mammaire (post-pubertaire)

et le syndrome mental présenté par notre petite malade. La littérature des perturbations endocriniennes, morphologiques et fonctionnelles, au cours des états schizophréniques est riche et très inégale quant à sa valeur. Nous nous contentons de renvoyer le lecteur au travail de *J. Müller*, inspirée par le prof. *M. Bleuler* de la clinique psychiatrique de Zürich. En l'état actuel de nos connaissances fragmentaires concernant les para-morphoses endocriniennes et les états mentaux pathologiques, nous devons nous contenter de signaler des faits, avant de pouvoir en proposer l'explication valable.

Peut-être, dans le cas de notre malade, la consanguinité parentale, l'éthylisme paternel, la syphilis extrêmement probable des géniteurs, explique-t-ils, en partie tout au moins, *et* la macromastie *et* le syndrome mental. Nous n'osons pas l'affirmer, car, il est difficile d'expliquer dans ce cas, pourquoi le petit frère de notre malade, qui est porteur du même agrégat de tares, ne présente aucune perturbation pathologique importante.

Résumé: Nous présentons l'observation clinique et le profil psychologique au test de Rorschach, d'une jeune fille de 17 ans, présentant un syndrome schizophrénique, chez laquelle nous avons noté une macromastie très importante. Discussion de ce stigmate, chez les malades mentaux, relativement peu signalé dans la littérature spécialisée.

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MYOCLONIA HEREDITARIA MUSCULI MENTALIS

By

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Apart from Unverricht's familial myoclonus epilepsy and Lenoble & Aubineau's familial nystagmus myoclonus there seem to be no other unquestionable forms of myoclonus which may be convincingly supposed to be based on hereditary conditions, but this may perhaps to some extent be due to the fact that other existing cases are of so benign a character and so harmless a form that medical assistance is not considered necessary.

The following is a report of a hereditary myoclonus syndrome which has been pointed out by a mother—who during her girlhood was the object of teasing on the part of other children because of this syndrome; she is now seeking medical advice, as she has two children who display the same syndrome and she would be sorry to see her children be exposed for this reason to the same teasing as she had to go through.

The symptom in question consists in fine but rapid myocloniae in the regio menti and they may persist from a few minutes to half a day. Other groups of facial muscles are not involved; the myocloniae of the musculi mentalis do not affect the lower lip, and are not coupled either with sensitive accompanying phenomena.

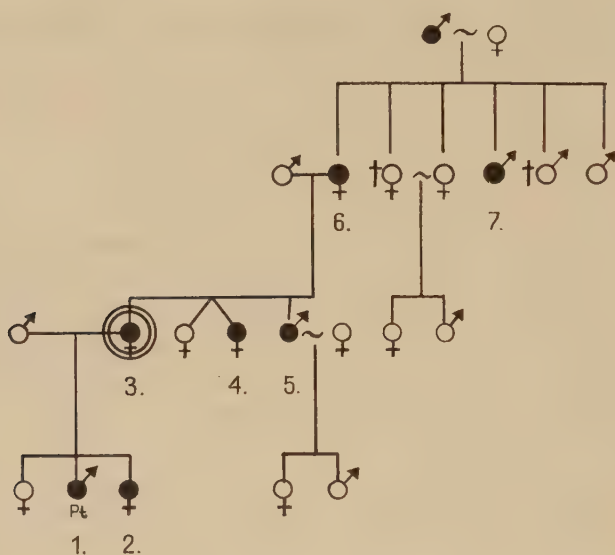
The said symptom seems largely to be rather monosymptomatic, but is, on the other hand, markedly hereditary.

Both females and males may be affected by this disease, which seems to be capable of transmission through males as well as females, as appears from the pedigree reproduced below:

The parents have noticed that the syndrome occurs as early as in the second or third week of life in the children (Nos. 1 and 2). The myoclonia appears and disappears independently of weeping or

laughter but may frequently be started if the children are highly occupied by some plaything.

From her earliest childhood the mother (3) also suffered from myocloniae of the regio menti—the symptoms persisted throughout her girlhood, and both among playfellows and at school she was very often exposed to so rude teasing that she recalls it with the utmost bitterness; this teasing has actually psycho-traumatized her during womanhood, too.



At the age of 15 years or so, the mother, who is now 28 years of age, began to suffer from epilepsy but has not really been treated for this disease—has not been in hospital either. When epilepsy supervened, the tendency to myocloniae of the regio menti decreased. The seizures may come on at any time during the 24 hours, there is no preceding aura, no biting of the tongue, but now and again the urine is passed. She may be unconscious for 4 or 5 minutes, but is in complete well-being when she wakes up again; there are no post-paroxysmatic pareses, but for some minutes and up to 30 minutes immediately after the universal seizure, there are persisting myocloniae of the regio menti. The seizures occur at intervals of weeks or months and without any known relation.

The mother conveys an impression of being normally gifted and is completely void of “epileptic manner”.

The neurological examination revealed nothing unquestionably abnormal.

The mother has two twin sisters who do not at all resemble each other, but one of the sisters (4) also suffers from myocloniae of the regio menti.

The mother's brother (5) also suffered from myocloniae of the regio menti, but at the age of 13 or 14 years he received a violent blow to this chin at boxing, after which the myoclonia disappeared. The muscoli mentalis must undoubtedly be supposed to have been so emphatically injured that there has been no anatomical basis any more for myocloniae of the muscle.

From her earliest childhood the maternal grandmother (6) has also been afflicted with myocloniae of the regio menti, and no appreciable change of this condition is said to have taken place in the course of time.

The maternal grandmother's brother (7) who is unmarried, also suffers from myocloniae of the regio menti.

It is told in the family that the maternal grandmother's father suffered from the same affection.

I did not succeed in tracing other peculiarities or abnormalities in the family.

SUMMARY

The writer gives a description of a hereditary form of myoclonia muscoli mentalis which occurs both in males and females and can be transmitted through males as well as through females.

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*Letter to the Editor concerning the article of Dr. Rich. Malmros:
A Simple Method of Producing a Special Picture of the Posterior
Part of the Third Ventricle.*

Dear Sir,

Receiving Vol. XXIV, Fasc. 3 and 4, 1949, of the *Acta Psychiatrica et Neurologica*, I was very astonished to read the article by Dr. Malmros: "A simple method of producing a special picture of the posterior part of the 3rd ventricle" pp. 587-597, in which the method has been described by me 2 years ago in the *Revue Neurologique*, tome 79, no. 7, 1947. I include a copy of this paper.

I suppose that Dr. Malmros was not informed of this publication, though it appeared in one of the current neurological Journals, but nowadays we know that before communicating a method or a conception as a new one, a searching investigation of the literature is more than ever obligatory.

I hope that you as the Chief Editor of the *Acta* will approve my demand to publish a note in the next number correcting this error, as justified.

Very sincerely yours,

H. Verbiest,

Chief of the Neurosurgical Dept. of the University of Utrecht, Holland.

Answer from Dr. Rich. Malmros.

In a letter to the editor Dr. H. Verbiest (Utrecht) has claimed that he two years before the publication of my paper has described the same method: *Le remplissage isolé d'air de la partie postérieure du troisième ventricule dans les obstructions de l'aqueduc de Sylvius. Revue Neurologique, tome 79, n° 7, 1947).*

In reply to Dr. H. Verbiest's letter I wish to state as follows: My paper was read on the first meeting of the Scandinavian Society of Neurosurgeons in Copenhagen on February 22nd—23rd 1946. On that occasion the figs. 3-4 and 19-21 amongst others were shown as lantern slides, after which the paper was laid aside as I did not wish to publish

it in print before I had got further experience. At that time (February 1946) my method was adopted by Professor Busch (Copenhagen). In January 1946 I went through the literature, but found nothing resembling my mode of procedure. On sending my paper to press in 1949 I was completely ignorant of Dr. Verbiest's publication. Had that not been so I should naturally have mentioned that the same happy idea had occurred to Dr. Verbiest and that Dr. Verbiest had published his experiences in the *Revue Neurologique* tome 79, n° 7, 1947.

R. Malmros,

Chief of the Neurosurgical Dept. of the University of Århus, Denmark.

BOOKS RECEIVED

F. M. R. Walshe, M.D.:

THE STRUCTURE OF MEDICINE AND ITS PLACE AMONG THE SCIENCES

The Harveian Oration.

E. & S. Livingstone Ltd., Edinburgh. 1948. 26 pag.

Wilhelm Bitter:

DIE ANGSTNEUROSE

Entstehung und Heilung.

Mit 2 Analysen nach Freud und Jung.

Verlag Hans Huber, Bern. 1948. 191 pag. Pr. Schw. Frcs. 9.80.

THE 1948 YEAR BOOK OF NEUROLOGY, PSYCHIATRY AND NEUROSURGERY

NEUROLOGY: Edited by *Hans H. Reese, M.D.* (Professor of Neurology and Psychiatry, University of Wisconsin Medical School) and *Mabel G. Masten, M.D.* (Associate Professor of Neuro-psychiatry, University of Wisconsin Medical School).

PSYCHIATRY: Edited by *Nolan D. C. Lewis, M.D.* (Director, New York State Psychiatric Institute and Hospital, Professor of Psychiatry, Columbia University).

NEUROSURGERY: Edited by *Percival Bailey, M.D.* (Professor of Neurology and Neurological Surgery, University of Illinois). The Year Book Publishers, Inc. 304, South Dearborn Street, Chicago. 750 pag. \$ 5.00.

Tore Broman:

THE PERMEABILITY OF THE CEREBROSPINAL VESSELS IN NORMAL AND PATHOLOGICAL CONDITIONS

From The Neurological Clinic of the University, Lund.

Ejnar Munksgaard, Copenhagen. 1949.

J. de Ajuriaguerra et H. Hécaen:

LE CORTEX CÉRÉBRAL

Étude Neuro-Psycho-Pathologique.

Préface du Pr. J. Lhermitte.

Masson et C^{ie} Éditeurs, Paris. 1949. 406 pages, avec 51 figures.

Raymond Garcin et Maurice Pestel:

THROMBO-PHLÉBITES CÉRÉBRALES

Masson et C^{ie}, Éditeurs, Paris. 1949. 144 pages, avec 29 figures.

Bibliothèque de Psychiatrie.

Pierre Pichot:

LES TESTS MENTAUX EN PSYCHIATRIE

Instruments et Méthodes.

Presses Universitaires de France, Paris. 1949. 238 pag.

Werner Bärtschi-Rochaix:

MIGRAINE CERVICALE

Das encephale Syndrom nach Halswirbeltrauma.

Mit 16 Tabellen und Kurven und 51 Abbildungen.

Medizinischer Verlag Hans Huber, Bern. 1949. Pr. Schw. Frs. 21.80.

W. Morgenthaler:

DIE PFLEGE DER GEMÜTS- UND GEISTESKRANKEN

II Band. 5. Aufl.

Medizinischer Verlag Hans Huber, Bern. 1949. 334 pag.

Pr. Schw. Frs. 30.00.

Eugen Bleuler:

LEHRBUCH DER PSYCHIATRIE

Achte Auflage umgearbeitet von M. Bleuler. Unter Mitwirkung von

J. Berze, H. Luxenburger, Fr. Meggendorfer, S. Scheidegger.

Springer-Verlag, Berlin 1949. 70 Abbildungen, 506 pag. DMark 26.00.

FESTSCHRIFT

zum 70. Geburtstag von Prof. Dr. Otto Pötzl.

Herausgegeben von Prof. Dr. Hubert J. Urban.

Universitätsverlag Wagner. Innsbruck. 1949. 464 pag.

Lucio Bini—Tullio Bozzi:

LA SCHIZOFRENIA

Nosografie e Teorie Generali.

Abruzzini Editore, Roma. 1949. 104 pag.

Folke Henschen, M.D.:

MORGAGNI'S SYNDROME

Hyperostosis Frontalis Interna Virilismus, Obesitas.

Oliver & Boyd Ltd., Edinburgh. 1949. 172 pag. 30 s.net.

Juan J. López Ibor:

LOS PROBLEMAS DE LAS ENFERMEDADES MENTALES

Corrientes actuales del pensamiento psiquiátrico.

Con 12 figuras.

Editorial Labor, S.A. Barcelona. 1949. 349 pag.

SUPRAVITAL ANALYSIS OF DISORDERS IN THE CEREBROVASCULAR PERMEABILITY

IV. Studies of the Technique and a Survey of Some New Results

By

TORE BROMAN, STIG RADNER, and LAWE SVANBERG
(Lund)

Disorders in the permeability of the cerebral vessels are probably an important pathogenetic factor in various diseases and pathological conditions. The ordinary anatomico-pathological examination of a brain does not disclose *direct* evidence of such a disturbance, but several morphological criteria may be produced in certain cases for such an assumption, e.g. a maximal distension and engorgement of the smaller veins and capillaries, signs of stasis, degenerative changes or complete necrosis of the vessel wall, distension of the perivascular spaces, often with serous fluid, petechial hemorrhages, and perivascular necrosis of the brain tissue. *Scheinker* recently described a number of pathological conditions displaying this histopathological picture and designated them "vasoparalysis" (1944, 1945, 1947).

The ordinary technique applied to experimental animals to show the existence of a disturbance in the vascular permeability of the brain, cannot of course be employed agonally in man. When animal experiments revealed that, as far as special dye-stuffs are concerned, the cerebral vessels keep their permeability unchanged a short time post mortem, the way was open for experimental studies of human brains (*Broman*, 1938, 1940). Such examinations were made and with positive results (*Broman*, 1944, 1947). For example, a distinctly discernible passage of the dyes through the vascular walls into the cerebral tissue was demonstrated in different kinds of brain tumours, in regions of cerebral edema, in the plaques of multiple sclerosis, and perifocally around massive hemorrhages and softenings. The present investigation constitutes a continuation of the above studies.

Earlier experience showed that the method is impaired by a number of considerable sources of error, and that several findings could not

be interpreted. For example, sometimes and for no apparent reason the brain stem stained conspicuously. Furthermore, a number of vessels, especially in the cortex, turned blue in a manner unknown in animal experiments—a phenomenon, however, apparently not due to a disorder in the vascular permeability, the dye being confined to the vessels or their contents. In most cases more or less numerous, distinctly stained dots or patches obviously due to a bulk escape from short limited sections of the vessels were discernible in the cortex of the hemispheres. In the subcortical white matter well-defined perivascular and strongly stained patches of different size were manifest—a specially common occurrence in the surroundings of edematous regions, and therefore suggestive of a commencing edema. It was proved that these patches, as well as the edematous regions, did not stain well by myelin sheath stains, a fact that was interpreted as evidence of their intravital origin. A further argument of this assumption was that (as was also the case with the above-mentioned lesions of the cortical vessels) they were sometimes attended by an escape of blood corpuscles into the perivascular tissue. The conditions responsible for their occurrence were, however, obscure.

On account of the above obscurities we deemed it necessary to perform control examinations in order, if possible, to find an explanation of the suspected artefacts. For this reason the present investigation is especially a study of the technique. Similar investigations were simultaneously performed in experimental animals by one of us (*Broman 1950*).

A. A CRITICAL STUDY OF THE TECHNICAL PROCEDURE ESPECIALLY WITH RESPECT TO INHERENT SOURCES OF ERROR

The technique adopted was on the whole the same as that described in previous papers (*Broman 1944, 1947*). As soon as possible post mortem the brain was removed and submerged in water. Cannulae were introduced into the carotid arteries and the basilar artery and were connected with rubber tubes to a container placed about one metre above the brain. The cerebral vessels were then perfused about 10 minutes with an 0.15 p.c. solution of trypan blue (in a saline solution). Afterwards the vessels were rinsed with a saline solution to wash away the dye, and finally a 10 p.c. solution of formalin was poured through to fix the brain.

1. *Control of the efficacy of the rinsing of the vessels*

The result was controlled microscopically in every case with a view to checking whether all the blood constituents had been washed out. Thick sections ($300\ \mu$) were cut from pieces taken from different parts of the brain. These sections, which were made transparent but not subjected to subsequent staining, were then examined.

In every case the grey matter of the cortex and the basal ganglia turned slightly but distinctly blue macroscopically. The microscopic inspection revealed that this colour was attributable not to a passage of the dye out into the brain tissue but to the fact that a varying number of blood vessels were stained blue (the majority, however, were unstained). These observations tallied well with previous experiments (*Broman* 1944, 1947). A close study of the frozen sections, however, showed that the stain was confined to the contents of the vessels. In some vessels the stained contents filled the whole of the lumen, and in such cases it was impossible to ascertain whether the dye had stained the vascular wall, too, but in other vessels the contents were reminiscent of a cobweb-like reticle adherent to one side only of the vascular wall, the other side being distinctly unstained. A few vascular branches completely unstained and filled with blood cells were also found.

A similar result is never found in experimental animals if the dye perfusion is performed within a short time post mortem. In these experiments the brains remain completely unstained, just as if the dye had been given in vivo (*Broman* 1941). If, however, a total or sub-total stoppage of the cerebral circulation is artificially produced by clamping the cranial arteries during a certain period before the animal is killed, exactly the same result will be obtained as in the supravital examination of human brains, the grey matter being slightly coloured macroscopically by the stained contents of vessels which have not been washed out (*Broman* 1950). It seems conceivable that the insufficient cerebral circulation during agony may be the cause of this phenomenon. Furthermore, a rapid post mortem coagulation of the blood is likely to occur in cases of prolonged agony. During the post mortem perfusion some of the dye solution presumably forces its way into the partially blocked blood vessels and accelerates the coagulation process, the subsequent rinsing with saline solution not being able to wash out the stained vascular contents.¹

The stained vascular contents probably consist of coagulated blood

¹ Recently *Broman* (1949) has modified the method, starting the perfusion with heparin, thereby avoiding the appearance of stained vascular contents.

plasma (precipitated fibrin). The reason why blood vessels with stained contents occur in larger number in the grey matter than in the white matter (where they are also found) is not clear, but it is probably partly ascribable to the grey matter being more vascularized.

If we compare the staining due to stagnated coloured vascular contents with that due to a real vascular lesion, we shall notice a conspicuous difference. In the latter case a microscopic inspection reveals a more or less marked perivascular staining. As a source of error the intravascular staining therefore plays no significant role in the supravital examination of the permeability of the cerebral vessels.

2. *The significance of traumatization in association with the removal of the brain*

For obvious reasons it is impossible to perform post mortem perfusion of dye into a human brain in situ. It must first be removed. In connection with this step a certain deformation and traumatization is unavoidable, and it is quite conceivable that such manipulations damage the vascular walls. The parallel series of animal experiments (*Broman* 1950) showed that mechanical compression of the brain is liable to rupture the vessels with a consequential passage of blood corpuscles and dye (during the perfusion) into the perivascular tissue (in the form of distinct spots).

In practically all the brains in the present as well as in the previous investigations (*Broman* 1944) intensely stained spots were found scattered in the cortex. In a few cases of the present material the brain was deliberately massaged in connection with its removal, with the resultant manifestation of a large number of such lesions of the cortical vessels. With a view to obtaining more convincing evidence, the brain was in some cases damaged traumatically only within a special cortical area, the rest of the brain being handled with the greatest care, and it was found that similar lesions of the cortical vessels occurred at the very site of injury, but not in any other part of the brain. A microscopic inspection of the damaged cortical vessels showed a marked escape not only of the dye but often also of blood cells.

We may thus conclude that mechanical compression of the brain leads to lesions and ruptures of some small superficial vascular branches and that the traumatization of the brains in connection with their removal is responsible for the manifested vascular damage.

In the white matter distinct, blue patches were observed around

the sections of some vessels. As a rule, such patches were more often visible in brains whose cortical vessels had been damaged extensively. It may therefore be presumed that the escape of the dye is due to vascular traumatization during autopsy and ought not to be considered a sign of a commencing multicentric cerebral edema, as was formerly supposed (*Broman 1944*).

With a view to producing a mechanical lesion of the vascular branches of the white matter, a few ml of saline solution were injected in a definite area of the brain both before and during the post mortem perfusion of the dye. At the site of these injections the white matter was damaged, displaying a distinctly stained peripheral zone about 0.5 cm in breadth. In the vicinity of this zone a number of small patches of the above type were also distinguishable. This supports the assumption that a mechanical injury during autopsy may cause vascular lesions also in the white matter, which, however, differ from similar lesions of the cortex in so far as the dye spreads more extensively in the white matter and hugs the vessels for a longer distance.

The fact known from earlier investigations that in histological preparations the myelin in such patches does not stain so readily was shown to apply also to the above-mentioned intentionally produced lesions. One may, therefore, presume that the post mortem imbibition of fluid changes the properties of the myelin in the same manner as does cerebral edema of intravital origin, and that these changes are responsible for the decreased stainability (that the presence of trypan blue does not interfere with subsequent myelin staining was shown previously; *Broman 1944*).

This source of error due to post mortem traumatization may effect the result severely. It is evident that the dye test reveals the existence of a derangement in the permeability of the cerebral vessels, no matter whether it occurs ante mortem or post mortem, for which reason it is of great importance to be able to discriminate between these two kinds of lesion. Although great caution in the removal of the brain may diminish this source of error, a certain amount of injury is unavoidable. It is worthy of note that these lesions have one distinct characteristic—they are restricted to a few single vascular branches and the leakage of the dye is always limited to a short section of the vessels.

Another conclusion that may be drawn in this connection is that when the brain is removed at ordinary autopsy, the presence of small scattered lesions of the blood vessels, which look like diapedesis-hemorrhages, but which in reality are due to post mortem trauma-

tization, is to be expected. Such small hemorrhages are of course more liable to occur when the blood is not completely coagulated at the time of autopsy.

3. *Control of perfusion technique*

Perfusion is occasionally impaired by an unsatisfactory flow of the solution through the cannulae. When this occurs, it is often due to too sharp a bend or torsion at the arterio-cannular junction. It may thus happen that dye-solution will remain in one of the rubber tubes and cannulae when perfusion with the formalin solution is started. This means that unless due care be taken, the dye and the formalin solutions will flow through the vessels simultaneously, with the result that owing to the injurious effect of the formalin on the vessels, the dye may diffusely escape into the cerebral tissue through the walls of the vessels. In animal experiments the simultaneous perfusion of the dye and the formalin solutions showed evidence of a wide-spread escape of the dye from the vessels.

This source of error, as is the case with the mechanical damage described in subchapter 2, is due to lesion of the vascular walls arising post mortem. But in this case the source of error is more serious because there is no essential difference between the passage of dye due to toxic lesions occurring post mortem, and that characteristic of a diffuse vascular injury in regions of edema of intravital origin.

This source of error may, however, be avoided or at least minimized by a careful observation of the flow through the cannulae during the change from saline solution (which is initially in the tubes connected to the cannulae) to dye solution and vice versa. As a rule, it is necessary to hold the cannulae with the hand the whole time, if a satisfactory flow is to be secured.

If in spite of these precautions a staining due to unsatisfactory flow is suspected, it is, however, possible to check whether this actually is the case or not. An area damaged diffusely intra vitam will always swell locally (edema), but this will not be the case if the injury is caused by the perfusion of the formalin. Analogously, we also find that the myelin stains in a normal manner in an area damaged by and during fixation, whilst the myelin in previously damaged regions will not stain so readily or so distinctly as in normal regions.

Essentially similar artefacts may be produced if the dye solution is not completely washed out owing to too brief a saline perfusion. However experience has shown that the quantity of saline solution used in our experiments (1-2 l/about 10 mins.) is sufficient thoroughly

to rinse the brain. It seems, however, probable that some of the dye solution may remain in the caudal part of the brain stem, which explains the diffuse staining of this region observed in many cases.

Another question is whether the supravital perfusion technique per se may not bring about further changes in the brain, so that the results are no longer comparable with what may be observed at an ordinary post mortem examination. First of all, the blood is washed out of most vessels, which, however, hardly need impair the evaluation of the results. In view of the fact that the perfusion pressure is kept below normal blood pressure, there is no risk of rupturing the blood vessels. As the dye and the saline solutions contain no colloids to prevent the escape of water from the blood vessels into the surrounding tissues, the perfusion may presumably cause an increase of the brain volume. The correctness of this assumption may be checked by weighing the brain both before and after perfusion or by recording the quantities perfused and quantity drained. An examination of brains with intact permeability showed the absorption of water and the increase in volume to be but slight (only a few per cent), probably ascribable to the brevity of the perfusion and the relatively low pressure applied. We thus found no reason to elaborate the technique in this respect by adding a colloid to the perfusion solution.

The result was quite different in cases with a wide-spread, diffuse disorder of the permeability with consequential cerebral edema, where the absorption of fluid was sometimes very pronounced. This was best illustrated by Case 8 with intoxication due to a hypnotic drug, in which prior to perfusion the arteries of one of the hemispheres were ligated. The cerebral hemispheres, which were initially of the same size, showed a marked difference after perfusion (about 25 p.c. difference in volume). A post mortem perfusion will thus evidently give an erroneous picture of the degree of the volumetric increase in cerebral edematous conditions. On the other hand, this post mortem absorption of fluid provides further evidence of the existence of abnormal conditions in the brain. It is, however, impossible to determine to what degree this increased absorption depends on the disorder in the permeability and how much it is dependent on the increased absorption capacity of the lesioned cerebral parenchyma. But it should be observed that we never found any increase of the brain volume without a simultaneous disorder in the vascular permeability (which argues against an addition of colloids to the fluid being able substantially to prevent the escape of water). In Case 4, for instance, in which an acute uremia was on the wane and in which, judging by the numerous punctate hemorrhages in the

Case No.	Diagnosis	Duration of agony	Fever	Hemorrh.	Disord. perm.	Site of disorder
1	Arterioscl. cerebri + Diabet. mellit. + Cirrhos. hepatis	long	—	0	0	—
2	Vit. org. cord. c. incompleta. + Embolia art. pulm.	short	+	0	0	—
3	Typhus exanthem. + Embolia art. pulm.	short	+	0	0	—
4	Glomerulonephritis ac. + Diabet. mellit. + Bronchopneumonia	short (uremia subsiding)	+	+	0	disseminated in the white matter
5	Nephrosclerosis malign. + Hypertonia + Uremia	long	+	0	0	—
6	Arsphenamine encephalopathy	long	+	+	+	entire brain (max. in the white matter and in the hippocampus)
7	Hepatitis ac. gravis	long	—	0	+	subcort. white matter and hippocampus
8	Barbitur. acid intox. + Bronchopneumonia	long	+	0	+	greater part of the white matter and hippocampus
9	Glioblastoma multiforme	long	+	+	+	within the tumour and perifocally
10	Cancer pulm. c. metastat. intracerebral.	long	—	+	+	the metastatic tumour and perifocally around the tumour and the massive hemorrhage

white matter, an extensive disorder in the vascular permeability evidently must have existed a few days before death (from supervening pneumonia), no substantial amount of water had been absorbed during perfusion.

B. SURVEY OF TEN CASES ANALYSED BY THE SUPRAVITAL METHOD

The present study comprises cases from the Medical Clinic, Lund. In all of these cases two or three arterial cannulae were inserted (in the basilar artery and in one or both of the carotides). The perfusion was commenced within two hours post mortem and in the most favourable case, already after one hour. After perfusion, the brains were properly fixed and a subsequent microscopical examination showed that in most cases the irrigation with a saline solution had been rather satisfactory.

The ten cases have been listed on page 128, the table showing the diagnosis, agonal conditions (where agony of long duration means $\cong \frac{1}{2}$ day, and fever + means $\cong 39-41^{\circ}$ C.), the presence of cerebral hemorrhages, and of a disorder in the permeability of the vessels attributable to a lesion caused in vivo by the disease.

1. Cases without cerebral lesions

In contradistinction to earlier investigations (Broman 1944, 1947) the present study comprises many cases that had not suffered from cerebral diseases. This makes it possible better to judge the method per se and relevant problems, because some of the cases may be considered as 'normals'.

Cases 1 and 2 may above all be regarded as 'normals'. The examination of the permeability of the cerebral vessels gave distinctly negative results (apart from typical mechanical vascular damage in a few regions). Case 3 with epidemic typhus was also negative, the histological examination of the brain (Prof. Ahlström) revealed nothing pathological, so that also this case may be accepted as 'normal' as far as the present investigation is concerned.

2. Extensive toxic lesions

Cases 4-8 may be considered examples of cerebral intoxication. Case 4 and 5 suffered from uremia. It is of importance to note that rather acute uremia occurred in both cases. In Case 4 it was obvious that a typical toxic lesion of the cerebral vessels had occurred (multiple punctate hemorrhages in the subcortical white matter), nevertheless

no disorder of the vascular permeability could be detected, which may be explained by the fact that the uremia had been subsiding considerably for already four or five days, when exitus occurred from a complicating bronchopneumonia. There is therefore every reason to assume that the cerebrovascular lesion had healed before the eximination (animal experiments have shown that toxic lesions of the permeability of the cerebral vessels may heal in less than one day, after elimination of the toxic agent; *Broman & Lindberg-Broman* 1945). In uremia experimentally produced in animals the punctuate hemorrhages stain distinctly blue if trypan blue is injected intravenously when the uremia is at its highest (*Broman* 1949). Case 5 exhibited no pathological cerebral changes whatsoever (examination complemented histologically with eosin staining and stains for myelin and lipoid), but this is no uncommon occurrence in acute uremia (*Knutson & Baker* 1945). For the purpose of the present study this case, too, may be considered as 'normal'.

Cases 6, 7, and 8 were all examples of existent toxic disorders in the permeability of the cerebral vessels. A characteristic common to all was that the damage was confined chiefly to the subcortical white matter and attended by signs of cerebral edema. It is also a well-known fact that cerebral edema exhibits a predilection for the white matter. The most probable explanation of this co-appearance is that the disorder of the cerebrovascular permeability is the cause of the edema (*Broman* 1944).

Case 6 (arsphenamine encephalopathy) presented the typical picture of 'vasoparalysis' as described by *Scheinker* (1944, 1947) with stasis, punctate hemorrhages, edema, perivascular demyelination, and necrosis of the tissue. A number of small vascular branches showed evidence of necrosis of the vascular endothelium besides which small hyaline thrombi had developed (histological examination was performed by Prof. *Ahlström*). In regions in which the stasis was most pronounced the stain was less conspicuous, which was a natural consequence of the fact that the dye solution was able to force its way through a few vascular branches only.

In Case 7 the toxic cerebral lesion was probably due to a serious disease of the liver from which the patient was suffering (the patient died in coma hepaticum). The immediate cause of this toxic lesion of the brain is obscure, but a correlation between serious diseases of the liver and lesions in the central nervous system has often been observed.

In Case 8 the toxic lesion was most probably somehow related to the prevailing intoxication. An explanation of this connection is, how-

ever, still unavailable. Barbiturate intoxication usually produces a general vascular dilation in the organism, which may possibly assume the nature of a real 'vasoparalysis'. In animal experiments in which heavy doses of hypnotics were given repeatedly during 6-8 hours no disorder in the permeability of the cerebral vessels was observed (*Broman* 1949). In the human case, however, the intoxication lasted 4 days, which may explain the stronger effect, but other explanations may also be imaginable (some form of endogenous intoxication in association with the prolonged coma?, picrotoxin treatment given throughout the whole of the four days?). Hyperemia and edema of the brain in cases of intoxication by hypnotics have been described earlier.

It may be of some theoretical interest to note that in all cases with toxic lesions the hippocampal cortex displayed a pronounced disorder in the vascular permeability, far more marked than in other parts of the cortex, and comparable with that of the white matter.

3. *Local cerebral lesions*

Cases 9 and 10 are examples of the conditions prevailing in local cerebral lesions. Both cases had malignant tumours that were found to possess vessels with permeability properties different from those generally met with in the cerebral vessels—they were permeable to the dye-stuff. This finding agrees with the results of earlier investigations (*Sorsby, Wright & Elkeles* 1943, *Broman* 1944, *Moore* 1948, *Moore et al* 1948). Furthermore, a disorder in the permeability of the vessels was manifest perifocally around the tumours and the massive hemorrhage caused by the carcinoma metastasis. Also this tallies with earlier findings (*Broman* 1944). The perifocal disorder in the vascular permeability is probably correlated to the circulatory disturbance peculiar to rapidly expanding processes and demonstrated by pathologists as local edema and multiple small hemorrhages.

The actual cause of this perifocal circulatory disturbance is still disputed. It is assumed by some to be toxic in origin, whilst others hold it to be due to congestion of the vessels. The latter view is supported by the fact that the perifocal lesions seem to be of the same type irrespective of the nature of the pathological process concerned (but more pronounced if it expands rapidly), and secondly, by experimental evidence showing that local venous obstruction may give rise to analogous vascular disturbances (experiments with brain hernias—*Broman* 1949). *Scheinker* (1945) in his study of the mechanism and development of the transtentorial herniation of the brain

stem also stressed the mechanical origin of the attendant local circulatory disturbance. On the other hand, there are also facts indicating that a massive tissue damage may have a toxic effect on the surrounding tissues, perhaps due to autolytic products (cf. the perifocal disturbance of the vascular permeability in cases of brain softenings, *Broman* 1944, in experimental animals subjected to massive circumscribed destruction of the brain, *Broman, Radner & Svanberg* 1949, and in necrotic areas due to carbon monoxide intoxication in man, *Broman* 1949).

4. *The effect of agonal factors in the cases examined*

In the experimental study mentioned above (p. 122) *Broman* analysed the effect of various factors that may come into play in the agonal stage. It was stated that anoxia of long duration does not disturb the permeability of the cerebral vessels, but that the arrest of the blood flow may initiate the intravascular clotting of the blood already *intra vitam* (cf. the effect of a delayed post mortem perfusion of the brain). Thus there is no reason to assume that the hypoxic conditions during a prolonged agony should disturb the vascular permeability, a presumption supported by the present investigation. On the other hand, however, a maximum raising of the cranial venous pressure or an extreme elevation of the body temperature was able to cause a slight disorder of the cerebrovascular permeability in animals. The question then arises what part these factors might have played in the results of the present investigation.

Case 2 suffered from a chronic general venous congestion (*vitium org. cordis*) and an acute increase of the venous pressure must have occurred in Cases 2 and 3 (exitus from pulmonary embolism), but apart from scattered blue dots in the hemispheres—probably artefacts due to traumatization of the brain at autopsy—no vascular lesions were observed. The experimental lesions caused by raising the venous pressure, appearing as scattered punctate hemorrhages, were mainly localized to the brain stem. Similar small hemorrhages have, however, been observed in human brains by *Berner* (1937), and *Dahl* (1937), and described by the latter as probably due to agonal venous congestion.

Elevation of the body temperature is a common agonal phenomenon. It is conceivable that the temperature sometimes might reach such a height (about 45° C. in brief experiments performed on animals) as to cause a disorder in the permeability of the cerebral vessels. In the present material, however, no correlation between the vascular disturbance and the final pyrexia could be shown. It is of course

possible that hyperthermia did play a contributory role in some of the cases with toxic lesions. In arsphenamine encephalopathy a marked elevation of the body temperature is said often to occur terminally (as also in our case). But the well-known picture of the cerebrovascular damage in this disease is indicative of its being of such long standing that it cannot reasonably be considered a resultant effect of a pyrexia that is not extreme until the last day; the high fever is usually also looked upon as a consequence of the cerebral lesion.

SUMMARY

1. The supravital method of demonstrating disorders of the cerebrovascular permeability in man was subjected to a critical analysis of (a) technical sources of error, and (b) factors apt to complicate the interpretation of the results.—Ten cases were examined and a brief report of the results is given.

2. As a rule the grey matter of the brain was of a diffuse bluish colour that macroscopically might be misinterpreted as a sign of disordered vascular permeability. Microscopically, however, the stain was confined to the blood contents remaining in a number of small vessels. This stagnation seems to be ascribable partly to the impaired cerebral circulation during agony, and partly to the unavoidable post mortem delay of the examination.

3. Artefacts may be produced by traumatization during autopsy and by a faulty perfusion technique. Maltreatment of the brain will damage a number of vessels with a consequent patchy escape of the dye around limitid sections of the vessels. Should the formalin solution come into contact with the dye solution the tissue may stain diffusely, in which case the staining may be difficult to distinguish from a lesion of intravital origin.

4. In brains with a disturbed vascular permeability the results obtained by the supravital method do not always correctly reflect the extent or degree of the intravital disturbance. In cases with a diffuse disorder of the vascular permeability and edema the perfusion will cause an appreciable further increase in the brain volume.—If, on the other hand, the vascular lesion is attended by pronounced stasis, the inflow of dye will be severely impeded and the region stained but slightly.

5. Such agonal factors as hypoxia, increased venous pressure, and fever did not seem to have any disturbing effect on the permeability of the cerebral vessels.

6. In cases of coma hepaticum, arsphenamine encephalopathy,

and acute barbiturate intoxication, a diffuse disorder in the vascular permeability was demonstrated, generally most marked in the sub-cortical white matter.

In a case of acute uremia subsiding for the last four days, the permeability of the cerebral vessels was completely normal, but multiple small hemorrhages of recent origin were indicative of a pre-existent disorder of the cerebrovascular permeability.

7. The authors were able to confirm earlier observations: (a) in brain tumours the presence of vessels with an abnormal permeability, and (b) around expansive processes the existence of a perifocal disturbance of the vascular permeability.

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CHRONIC POLYMYOSITIS

By

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The purpose of this work is to elucidate the clinical aspects of chronic polymyositis and to call attention to muscle biopsy as a means of differentiating myositis from other lesions of the muscles—to-day this point is of more than theoretical interest, as myositis now seems to be, at any rate in part, amenable to rational therapy.

We have, therefore, thought it would be useful to publish the following six cases of chronic polymyositis, which all had a considerable resemblance to other, mainly muscular, affections, and which were all first diagnosed erroneously.

The literature on acute and subacute myositis—or dermatomyositis, if the skin is also involved—is rather scattered. In 1887, independently of each other, *Wagner* (1887) described “Die Myositiden”, *Hepp* (1887), “Pseudotrichose”, and *Unverricht* (1887) “Polymyositis acuta”. In 1891, *Unverricht* described dermatomyositis. *Strümpel* (1891) mentions “Die primären acuten Polymyositiden”. Among other authors may be mentioned *Plehn* (1889), *Boeck* (1891), *Lewy* (1893), *Löwenfeld* (1890), *Waetzold* (1893), *Senator* (1893), *Schultze* (1895), *Köster* (1898), *C. Otto* (1895), *Munthe Fog* (1919), *Heckscher* (1925), and *Erna Christensen & Renvig* (1945).

In the cases they have reported, the lesion was usually acute, and most often a dermatomyositis. Thus *Bohse & Benjaminsson* in 1943, also described a case of severe dermatomyositis as a reaction to cancer of the gall bladder. In 1948 *Grelland* reported a slowly progressive case of dermatomyositis with vascular disturbances and gangrene.

Chronic polymyositis without any skin affection, on the other hand, has been described more rarely. In 1898 *Cassirer* reported a case with pain, weakness and atrophy of the lower limbs, which was undoubtedly

an instance of polymyositis. *Cassirer* discussed this diagnosis, but thought that the condition was more probably a progressive muscular dystrophy. *Osler* (1909) mentions acute, subacute, and chronic myositis.

In 1937 *Ph. Levison* described two cases of polymyositis involving mainly the proximal muscles, in which the muscles were examined microscopically. One died of pharyngeal paralysis with edema of the glottis. In 1942 *E. Krabbe* published a case in which dermatomyositis was, it is true, present, but was combined with pronounced atrophy of the proximal muscles. In 1945 *Furtado & Alvim* published two cases of polymyositis which closely resembled progressive muscular dystrophy. The diagnosis was confirmed by muscle biopsy. *Urechia* (1943) also described a case of polymyositis, and *Zetterholm* (1946) published a somewhat atypical case with eosinophilia, in which the possibility of trichiniasis could be excluded.

AUTHORS' OWN MATERIAL

Case 1. (Neurological Dept. of the Kommunehospital. Rec. no. 433/47).

Woman, single, aged 38 years. Family history negative as to muscular affection. Past history negative, but the patient had never had particular good muscular power in the arms.

For a year she had had gradually increasing pain in both thighs posteriorly, radiating at first down to the popliteal space, later to the calves and heels. Ambulant treatment with massage and injections of vitamin B had no effect. About 9 months earlier she was admitted to hospital for lumbar myosis, and improved with physiotherapy. During the last six months there had been gradually increasing muscular weakness, tiredness, and painful contractions in the lower limbs on walking, with gradual development of toe-walking, which to some extent prevented painful cramps in the calves; she had difficulty in going upstairs and in getting up from a chair, also slight dysphagia. For two months there had been increasing weakness of the arms, so that now the patient could not even cut her own food. She was still able to write.

Objective examination.

Cranial nerves and the muscles of the face and neck: no abnormality detected.

Vertebral column: normal when supine and when standing in her shoes, but the lumbar lordosis increased when the heels were put to the floor.

Upper limbs and trunk: considerable atrophy of the deltoid, supra- and infra-spinatus and pectoralis major; doubtful atrophy of the margins of the trapezius. Moderate atrophy of the biceps brachii, corresponding paralysis of all movements at the shoulder joint, and of the flexion of the elbow; extension of the elbow and hand grip were fairly strong. Normal tone. The triceps and brachio-radial reflexes were absent, the biceps reflexes faint. Normal sensation.

Lower limbs: no apparent atrophy; slight weakness of flexion of the hip; fairly good power at the knee; active dorsiflexion of the foot only to 90°. Tendon reflexes slightly reduced on the right side. Normal sensation.

Gait: toe-walking to avoid the painful contractions in the calf muscles, which appeared as soon as the heels were put to the floor. Unable to flex the knees actively when the heels were on the floor. Unable to mount stairs without support; able to get up from a chair only by using her arms; unable to get up from a supine position without first turning on to her side.

Repeated electromyography gave uncertain results.

Muscle biopsy: Varying degrees of atrophy of the muscle fibrils in the individual muscle fibres, rather marked interstitial edema, diffuse and especially perivascular, infiltration with lymphocytes, plasma cells, polynuclear leucocytes, some of which are eosinophil, and a few fibroblasts. The vessels are normal, without epithelial proliferation or affection of the walls.

Histological diagnosis: Polymyositis and muscular dystrophy of peripheral origin.

Laboratory examinations:

Hemoglobin: 100 %. Wassermann negative. Urine: no pathological elements.

Blood urea, serum chloride, and complete blood examination normal—apart from 4 % eosinophil leucocytes.

Sedimentation rate: 11-14 mm/1 hour. Creatinine index: 112.

After the muscle biopsy, penicillin therapy was instituted: 100,000 O.U. three times daily for 10 days (a total of 3 million O.U.).

Five weeks after admission the pulse became markedly irregular, and on the following day the patient had a severe Adams-Stokes' attack with forced respiration, fits, urinary incontinence, and transitory absence of pulse beats and heart sounds.

After this attack there was an irregular and slow pulse (under 50), which persisted.

During the following 3 weeks she had 17 similar attacks, though at increasing intervals.

Electrocardiography showed alternating bundle branch block.

Eight weeks after admission the patient died in a further attack.

Autopsy diagnosis: Moderate stasis of the organs; small left ovarian cyst; sequelae of pleurisy (slight).

At autopsy, specimens of tissue were taken for *microscopic examination* from the septum of the heart, left ventricle, triceps and biceps of the arm, quadriceps of the thigh, and liver.

Sections from the myocardium showed areas in many places of degenerated muscle, replaced here and there by plaques of round-cell infiltration and beginning connective tissue formation.

The striated muscles showed pronounced pathological changes in the form of diffuse infiltration with lymphocytes and large mononuclear cells, some of which were certainly plasma cells. The cell infiltration was most pronounced round the blood vessels. The interstitial connective tissue was increased, and there was edema of this tissue. The muscle fibrils showed varying degrees of atrophy in the individual bundle, and in many places the striation was effaced; vacuolisation was also seen here and there.

The liver showed moderate infiltration of the interstitial connective tissue with lymphocytes, and also moderate hyperemia; the liver cells are normal.

Histological diagnosis: Subacute polymyositis; subacute myocarditis; subacute hepatitis (mild).

Sections from various parts of the spinal cord show retrogressive ganglion-cell degeneration in the large motor cells of the anterior horn.

Summary of case:

A woman, aged 38 years, had complained for a year of increasing muscle pain and weakness, first of the lower, and later, also of the upper limbs. Physical examination showed muscular wasting of the shoulder girdle and some weakness and reduced mobility of the lower limbs. The creatine output of the urine was increased; muscle biopsy showed myositis. Penicillin treatment was instituted. Under this treatment the patient had alternating bundle branch block and she died in an Adams-Stokes' attack. Autopsy (microscopy) showed generalized subacute myositis, involving also the myocardium.

Case 2. (Neurological Dept. of the Rigshospital. Rec. no. 133/49).

Woman, married, aged 27 years. Family history negative as to muscular affection.

She had always had a marked lordosis, and the muscles of her back had never been very strong. For several years she had had difficulty in mounting stairs, and after her first pregnancy, 10 years ago, her legs, and in the last 18 months her arms also, had become increasingly weak; the weakness had progressed during her three pregnancies without improving in the intervals. There was slight muscle pain.

Objective examination:

Cranial nerves: no abnormality.

Neck: Weakness of both sternocleidomastoids, which are slightly atrophic.

Vertebral column and muscles of the back: Hyperlordosis of the lumbar spine; unable to get up from the supine position, only able to lift her head weakly. Flattening of the upper muscles of the back on both sides, especially the supraspinatus and rhomboids, but hypertrophy of the infraspinatus; slight winging of the scapula.

Upper limbs: Atrophy of the deltoid, serratus anterior and pectoral muscles with corresponding weakness of all movements in the shoulder joint. No atrophy or paresis. All tendon reflexes absent. Normal sensation.

Abdominal reflexes normal. Beevor's sign negative.

Lower extremities: Diffuse pseudohypertrophy. Cannot raise the lower limbs off the floor in the supine position. Free mobility in both knees; active knee extension good, flexion poor; active ankle movements, good power. Able to get up from a sitting posture only by pushing with her hands on her thighs. Patellar reflexes absent. Achilles reflexes moderate and equal on both sides. Normal sensation.

Gait: Waddling, with hyperlordosis of the lumbar spine. Unable to get up from a seat without help.

Muscle biopsy: Histological examination of 2 muscle biopsies—before and after treatment with streptomycin therapy—showed a uniform picture of perivascular infiltration with lymphocytes, macrophages, and fibroblasts, and a rather irregular atrophy of the muscle fibrils in the individual fibres—as usually seen in muscular dystrophy of peripheral origin.

Laboratory examination:

Antistreptolysin titre: 100 (normal). Differential count: normal, apart from 3.5 % eosinophil leucocytes.

Creatinine index in urine: 124-154 (increased).

Electromyography: suggestive of myogenous affection.

Sedimentation rate: 20—26—32—45—37 mm/1 hour. Wassermann negative. Hemoglobin: 86 %. Urine: No pathological elements.

During her stay in hospital she was treated with streptomycin, 50 cg. twice daily for 4 weeks, with two intervals because of dizziness. During treatment there was first a rise, then a fall in the sedimentation rate. Subjective as well as objective improvement of the power of flexion of the elbow and extension of the knee; now able to mount stairs without holding on to the rail.

Subsequent course: Apparently no further improvement in her condition.

Summary of case:

The patient was a married woman aged 27 years, who had always been troubled with hyperlordosis and for several years had had difficulty in ascending stairs. In connection with each of three pregnancies, the muscular power of the limbs decreased. There was dystrophy and paresis of muscles of the shoulder girdle, pseudohypertrophy of the musculature of the lower limbs, weak flexion of the hip and knee, absence of patellar reflexes, wadding gait, and slight pain in the muscles. The creatinine index of the urine was increased, the sedimentation rate slightly raised. Muscle biopsy showed polymyositis, combined with muscular dystrophy of peripheral origin. Slight improvement with streptomycin treatment.

Case 3¹. (Pediatric Dept. of Rigshospitalet, Rec. no. 566/49).

Boy, aged 9 years. Family history negative as to muscular affection. The mother had been well during pregnancy.

Birth by normal spontaneous delivery at term. Past history: good health. Soon after birth the boy was noticed to have flaccid flat-foot. He was late in walking (18 months) and was never able to run; able to ascend stairs only with difficulty. The muscular power of the arms was always poor. His condition had been rather stationary. No pain, but tenderness of the muscles.

Objective examination:

Normal height, thin. Mental habitus normal, quick perception.

Face and neck: No abnormality of the musculature.

Vertebral column: Pronounced hyperlordosis in walking.

Upper limbs: Joints free. Slight to moderate weakness of the shoulder girdle in all respects; moderate weakness of the flexion of the elbow, extension a little better; good grip. Slight or moderate atrophy of the supraspinatus, infraspinatus, teres, pectorales, deltoid, biceps, and triceps. Tendon reflexes fairly brisk and equal. Definite tenderness of the shoulder girdle.

Lower limbs: Joints free. Flat feet. Slight or moderate weakness of all movements at the hips and of flexion and extension of the knees. Doubtful atrophy of the musculature of the buttocks and thighs; moderate but definite pseudohypertrophy of the calves. Patellar reflexes weak; equal; Achilles reflexes fairly brisk

¹ This case will be dealt with separately in *Acta Paediatrica* by Claus Dueholm.

and equal. Plantar reflexes normal. Definite tenderness of the shoulder and femoral muscles on both sides.

Gait: Backwards tilt, waddling, metatarsal walk.

Gets up from floor by turning on his side and climbing up his legs.

No other neurological abnormality detected.

Laboratory examination:

Sedimentation rate: 8 and 7 mm/1 hour. Hemoglobin: 90 %. White blood count: 4920. Differential count: 58 % polymorphs, 2 % eosinophils, 40 % lymphocytes.

Tuberculin test (Moro, 72 hours): +. Antistreptolysin titre: 45 (normal). Venous blood culture: no growth (twice).

Preformed creatinine: 146 mg. Creatine: 62 mg.; 298 mg. in 24 hours (normal for children 0-350 mg.). Creatinine index: 136.

Radiography of the lumbar spine, pelvis, and lower limbs: no abnormality.

Electromyography indicated paresis of myogenic origin.

Electrocardiography: no abnormality.

Muscle biopsy, from the right calf: Areas of degeneration and effacement of the striation, especially in places with accumulation of lymphocytes and larger mononuclear cells in the interstitial tissue. No evidence of tuberculosis. Eosinophil cells seen in a few places in the interstitial tissue.

Histological diagnosis: Chronic polymyositis.

Treatment: Streptomycin treatment: 1½ g. the first day in six doses and 1 g. daily in four doses for eight days in two periods. During and after the streptomycin treatment, improvement in walking and getting up from the floor.

A further *muscle biopsy* after the streptomycin treatment showed irregularity of the muscle fibrils as before, no eosinophil leucocytes and only very little round cell infiltration.

Summary of case:

The patient was a boy, aged 9 years, with apparently typical progressive muscular dystrophy; the lesion had, however, been present since infancy and was not particularly progressive. Atrophy and paresis were not pronounced in the limbs; there was also pseudo-hypertrophy of the calves. Creatinine output in the urine was increased. Muscle biopsy showed myositis. During and after streptomycin treatment his walking and getting up from the floor improved. A new muscle biopsy showed very slight round cell infiltration.

Case 4. (Neurological Dept. of the Rigshospital. Rec. no. 41/49).

Girl, aged 16 years. Family history negative as to muscular affection. Past history of good health.

For 6 months she had suffered from general tiredness, increasing weakness and reduced mobility, pain on movement in the shoulders, upper arm, hip and thigh on both sides, and on flexion of the knee; difficulty in ascending stairs and in getting up from sitting and lying; and difficulty in swallowing fairly coarse particles. At first her illness was thought to be a polyarthritis.

Objective examination:

Skull and cranial nerves, facial and cervical muscles: no abnormality; no demonstrable weakness of the tongue and palate, though her speech is somewhat twangy and indistinct.

Vertebral column: Curvatures normal, mobility free. Some foci of myositis in the lumbar musculature.

Upper limbs: Range of movement in both shoulders and elbows slightly reduced owing to muscular pain. The muscles are generally thin, rather tender, probably slightly firmer than normal, slight diffuse weakness at the shoulder and elbow. Normal tone and sensation. Faint but equal tendon reflexes.

Abdominal reflexes equal and fairly brisk.

Lower limbs: Slight limitation of passive rotation of both hips; knee joints flex only to 90° in full flexion. Marked tenderness of the muscles of the lumbar and gluteal regions and thighs.

Gait: Waddling. Unable to get up from a supine position—even after turning over on her side.

Electromyography showed interference, no synchronization, which does not suggest neurogenic atrophy.

Muscle biopsy: Accumulation of lymphocytes in the interstitial connective tissue and amongst the muscle fibrils. Apart from the round cell infiltration, there is irregular atrophy of the muscle fibrils in the individual bundles—as in dystrophy of peripheral origin.

Histological diagnosis: Polymyositis with muscular dystrophy (secondary?).

Laboratory examination:

Hemoglobin 90 %. Urine: No pathological elements. Wassermann negative. Complete blood examination shows 5 % eosinophil leucocytes. Antistreptolysin titre: 250—400—320—360—280—180.

Sedimentation rates: 10—14—5—23—32—18—26—10—7—8 mm/1 hour.

Treatment: After the muscle biopsy, penicillin therapy was begun, 200,000 O.U. 3 times daily. After 24 hours, however, it had to be discontinued on account of a marked rise in temperature. One week later the penicillin therapy was continued, this time with 50,000 O.U. twice a day, which she tolerated without any inconvenience. After this, the dosage was gradually increased to 200,000 O.U. 3 times a day: the total dose was 4 million O.U. On discharge she moved about freely without any pain though still limping on her left leg. Good power of all the muscles, and no muscular tenderness.

After discharge she returned at intervals for control examination. The antistreptolysin titre rose to 560, the sedimentation rate to 17 mm/1 hour and the muscular pain returned. She was readmitted for streptomycin therapy.

Objective examination: 30° loss of full extension of the elbow. Still tenderness of the musculature of the upper extremities. Can raise straight legs to 45°. Free movement and good power in the lower limbs. Weak tendon reflexes, equal on the two sides. Still slight dragging of the left leg on walking.

Treatment: Streptomycin, 0.5 g. twice a day for 14 days through two periods. In direct response to this treatment, the antistreptolysin titre fell to 230; later, it again rose to 320. During treatment, the symptoms subsided, and the patient was discharged, feeling well, with a sedimentation rate of 7 mm., and an antistreptolysin titre of 310.

Subsequent course: No tenderness of the muscles, walking quite normal, movements of the joints free.

Examination 2 years later: Complete recovery (after careful training of the muscles).

Summary of case:

The patient was a girl, aged 16 years, who had for six months had an illness which clinically resembled polyarthritis; there was increasing tiredness, loss of muscular power and tenderness of the muscles of all four limbs. On admission the muscles were tender, but showed no atrophy; there was moderate reduction in the mobility of the various joints, suggesting rather a reaction to pain than any true joint affection; the antistreptolysin titre was raised, the sedimentation rate slightly raised. Muscle biopsy showed myositis; a complete blood examination showed a very slight degree of eosinophilia. Improvement under penicillin treatment. On readmission, recovery with streptomycin treatment.

Case 5. (Neurological Dept. of the Rigshospital. Rec. no. 171/49).

Woman, married, aged 35 years. Family history negative as to muscular affections. Cervical lymphadenitis as a child; several times an in-patient at the Kyst-hospital sanatorium. She has always been asthenic, ailing.

For a year she had a gradually increasing weakness, with sharp pains, aggravated by exertion. These pains first occurred in the right arm, later they were more generalised, though particularly marked in the shoulders and upper arms. The pains were worst in the morning.

Sedimentation rate two months before admission: 70 mm/1 hour.

Objective examination:

Skull and cranial nerves: no abnormality.

Vertebral column: normal. Diffuse tenderness of the back muscles in the lumbar region.

Limbs: All joints free; no weakness; musculature delicate throughout, especially in the right arm. Marked diffuse tenderness to palpation of all muscles. Tendon reflexes moderately brisk and equal; plantar reflexes normal. Sensation normal. Gait normal.

She was first thought to be a *nervous asthenic with diffuse myosis*. As muscular tenderness and pain increased, a *muscle biopsy was taken*; it showed perivascular accumulations of lymphocytes and large mononuclear cells round the larger vessels.

Histological diagnosis: Myositis.

Laboratory examination: Antistreptolysin titre: 80-90 (normal). Wassermann negative. Hemoglobin: 90 %. Urine: N.A.D. Blood pressure: 110/70. Complete blood examination: normal findings.

Sedimentation rate: 27—50—18 mm./1 hour.

Treatment: Tonics, sedatives, and antineuralgics, and for 7 weeks penicillin 200,000 O.U. three times daily—a total of 400 million units. During treatment the sedimentation rate fell from 60 to 34 mm.

Afterwards, there was a slight, gradual aggravation of the symptoms, and 6 months later two 14-day courses of streptomycin (0.5 g. twice a day) were given.

Sedimentation rates: 14-12 mm./1 hour during the streptomycin treatment.

Muscle biopsy, after the streptomycin treatment, showed only very slight peri-

vascular infiltration with lymphocytes, but there was slight irregularity in calibre of the muscle fibrils, as seen in early muscular dystrophy of peripheral origin.

Subsequent course: The muscle pain decreased.

Summary of case:

The patient was a woman aged 35 years, who had always been asthenic. For a year there had been increasing muscular weakness and muscle pain, first in the right arm, later more generalised. There were generalised muscular tenderness and a raised sedimentation rate. The first biopsy showed myositis; later—after treatment with streptomycin—the picture corresponded with that of a beginning muscular dystrophy of peripheral origin. She was treated first with penicillin (altogether 400 million O.U.), later with streptomycin (total dose of 28 g.).

Case 6. (Neurological Dept. of the Rigshospital. Rec. no. 672/49).

Man, aged 41 years, with a negative family history as to muscular affections.

For 10 years he had suffered from diplopia, corrected by the use of glasses. 9 years ago there had been a sudden onset of painful ptosis of the right eye-lid; after a few months it subsided a little and has since remained unchanged.

Six years ago, a sudden onset of weakness of the right arm; since then, occasional similar attacks, lasting for about half an hour, involving both hands, particularly the left one, at intervals of a few hours. For one month, muscular weakness of the legs on running or climbing stairs, localised especially to the left quadriceps. In addition, tiredness of the jaws on mastication of hard food. During the last days before admission in 1946, pain in the occipital muscles with movement.

Objective examination:

Cranial nerves: bilateral ptosis with compensatory wrinkling of the brow (paralysis of the rectus superior, moderate paresis of the rectus lateralis and slight paresis of the rectus medialis), atrophy of the masseter.

Upper limbs: Joints and tone normal; atrophy of the triceps, with corresponding weakness of extension of the elbow; tendon reflexes moderately brisk and equal.

Abdominal reflexes: moderately brisk and equal.

Lower limbs: No abnormality.

Gait: normal; able to get up from supine position without using his hands.

Muscle biopsy (from the right triceps) shows lymphocytic infiltration, in particular perivascular in the interstitial tissue, extending inwards round the individual muscle fibrils, many of which show varying degrees of atrophy. There is no regular distribution of the atrophic muscle fibrils in the individual bundle.

Laboratory examinations: Spinal fluids (Fuchs-Rosenthal); 2/3 lymphocytes; globulin: 2; total protein: 20 (slightly increased) (Bisgaard's method). Wassermann negative. Hemoglobin: 100 %. Sedimentation rate: 3 mm./1 hour. Urine: No pathological elements.

Treatment and course: Improvement with myotensor treatment. After discharge, treated with prostigmine tablets, with good effect.

On *readmission*, in 1948, after staying in another hospital, the patient complained of pronounced tiredness and increasing, now permanent, weakness of all limbs and sudden increased weakness which might make him fall. He was unable to cut up his meat; had difficulty in dressing and undressing, and in masticating. His symptoms were more pronounced in cold weather; there was sometimes fibrillation.

Objective examination:

Speech somewhat nasal; no change in the paresis of the eye muscles; slight atrophy of the facial muscles, with reduced power in puffing out the cheeks; bilateral atrophy of the masseters; some weakness of the sternocleidomastoid.

Upper limbs: moderate atrophy of the pectoral muscles; slight atrophy of the deltoid, triceps, and biceps—all with corresponding weaknesses. In addition, weakness of the digits, in spite of absence of any apparent atrophy.

Tendon reflexes hyperactive, with preponderance of reflexes of the right side; slight diffuse muscular fibrillation; weakness of hip movements, flexion of the knees and dorsiflexion of the foot. Tendon reflexes brisk. Plantar reflexes atypical.

Gait: Walked with stiff legs. Unable to sit up without using the hands.

Treatment: Again favourable results with prostigmine tablets.

Muscle biopsy, performed in February 1947—during the stay in another hospital—shows patchy atrophy of the muscle fibrils in the individual bundles, but no round infiltration. This finding is more suggestive of dystrophy of central origin, even though the patchiness seems to suggest remnants of focal inflammatory processes.

Muscle biopsy of 5/4/48 shows irregular atrophy of the muscle fibrils as in muscular atrophy of peripheral origin. This specimen also shows no round cell infiltration.

Readmission in 1949 for threatening diabetic coma (diabetes has developed since the preceding discharge).

Muscle condition as in 1948.

Summary of case:

The patient was a man, aged 41 years, who for 10 years had been troubled with a muscular affection, which had begun as painful pareses—e.g. painful ptosis of both eyelids; later general permanent weakness with rapid tiring developed. The c.s.f. showed an increase in total protein on one occasion. The sedimentation rate was normal. His condition improved with prostigmine tablets.

In 1945, muscle biopsy showed myositis with dystrophy of peripheral origin; in 1947, dystrophy, mainly of central origin, though perhaps remnants of focal processes, and finally—in 1948—dystrophy, mainly of peripheral origin. In 1947 and 1948 there was no round cell infiltration, i.e. no features suggestive of myositis.

DISCUSSION

From these case records it is evident that none of these patients presented any skin affection—that is, dermatomyositis—which might

give rise to the same diagnostic problems. The introductory survey of the literature has shown that dermatomyositis has been described far more frequently than myositis (polymyositis) without skin affection. Further, unlike cases of neurodermatomyositis, in which peripheral nerve branches are also involved, with various disturbances of sensation, our patients had no disturbances of sensation.

A glance at the case records shows that the symptomatology may be somewhat varied.

In cases 1, 2, and 3 the clinical picture was almost indistinguishable from that of progressive muscular dystrophy, with proximal atrophy and weakness of the limb muscles and the typical waddling gait. In cases 1 and 2, however, the condition appeared rather late in life (at the age of 38 and 22 years, respectively), whereas in case 3 the lesion had apparently been present for 9 years since birth. It is to be noted that in case 1 there was more pain in the legs and loins than is usual in progressive muscular dystrophy, and also some difficulty in swallowing. In case 3 there was unmistakable tenderness of the shoulder and thigh muscles. In case 2 there was less pain.

In cases 4 and 5 the muscle pain was the most marked symptom. Although case 4 showed proximal atrophy and pareses, her main symptom was pain and stiffness round the shoulder, elbow, hip, and knee joints, not, as in arthritis—with which the lesion was at first confused—due to an affection of the joints themselves. There was also slight tension in the tender muscles surrounding the joints, and there was slight dysphagia.

In case 5 the muscle pain mainly affected the upper limbs, particularly the shoulders, but later it became more diffuse; at first the lesion was thought to be a myosis, though there was more spontaneous pain at rest than usually encountered in ordinary myoses: further, the affected muscles involved were tender to touch.

In this connection three further cases may be mentioned: two had severe spontaneous muscle pain in the shoulder girdle and hip region; later there was slight atrophy; there was a considerable rise in the sedimentation rate, an initial subfebrile temperature, the condition was aggravated by massage; the diagnosis of myositis was made on the clinical picture. In a third case there was atrophy and pain in the muscles of both shoulders after the patient had had an inflammation of a finger. Now he seems to be cured by treatment with Streptomycin.

Case 6 presented the most varied clinical pictures: with general tiredness and muscular weakness, a rather sudden onset of painful ptosis and diplopia, and weakness of mastication. This patient was severely disabled for 7-8 years by the general muscular weakness, but

had no particular pain. Atypical progressive muscular atrophy was diagnosed first, later myasthenia gravis was thought to be more likely.

In all cases the family history was negative as regards muscular affections. Nor was there any suggestion of a precursory infectious stage.

In cases 2, 4, and 5, and in the two further cases mentioned above, the sedimentation rate was raised.

In one patient (no. 4) the antistreptolysin titre was raised.

Blood cultures were negative in five (no. 1-5) cases.

The creatinine output was raised in cases 1-4, normal in case 5 (there was no demonstrable muscular atrophy in this case); it was not examined in case 6.

Electromyography was performed in all the cases except no. 5; the findings indicated a myogenic affection¹.

Complete blood examination was performed in cases 1-4 and showed no abnormality, apart from a slight tendency to eosinophilia (maximum 5 %), though less than in Zetterholm's (24) case (32 %).

The only feature common to all six patients, and on which the diagnosis of polymyositis was made, was the outcome of the *muscle biopsy*, which in all six patients showed inflammatory infiltration in the interstitial connective tissue. In case 1 the sections showed polynuclear leucocytes (some of which were eosinophil), lymphocytes, plasma cells and histiocytes. In cases 1, 2, 5, and 6 the round cell infiltration was preponderantly perivascular, while in the remaining 2 cases it was diffuse. The muscular fibrils in the individual bundles showed irregular atrophy, as in dystrophy of peripheral origin.

In case 5 a new muscle biopsy taken after treatment with streptomycin showed no inflammatory changes, but merely the usual picture of muscular dystrophy of peripheral origin.

In case 6, also, the inflammatory changes had disappeared on subsequent biopsies (respectively 2 and 3 years after the first examination), leaving features of peripheral muscular dystrophy.

Recapitulation.—Among the 6 cases of polymyositis here reported, 3 showed a pronounced clinical resemblance to progressive muscular dystrophy with proximal atrophy and pareses (also pseudo-hypertrophy). 4 cases (excluding 2 cases not described here) had spontaneous pain, mainly in the proximal muscles. *Cassirer* (1898), *Furtado Alvim* (1945), and *Ph. Levison* (1937) also found that the lesion was localised chiefly in the proximal muscles. In case 6, on the other hand, the localisation was atypical.

¹ Later *Buchthal & Pinelli* have found action potentials of an abnormally short duration in all cases of polymyositis and in some non hereditary cases of progressive muscular dystrophy, in which interstitial infiltration also was found.

As will be seen, it is mainly the proximal muscle groups which are attacked. This, however, must be looked upon as common to various myogenic muscular affections (in particular, progressive muscular dystrophy) in contrast to muscular affections of neurogenic and spinal origin. No adequate explanation of this is yet available, but it may be mentioned that *Babinski & Onanoff* (1888) have demonstrated that the proximal muscles develop before, and the distal muscles often after the fifth foetal month.

Etiology.

The etiology is still quite obscure. In one patient (no. 4) the anti-streptolysin titre was found to be raised without any demonstrable focus. In the remainder the cause was completely unknown. Presumably, however, the muscular affection may arise in response to various endogenous as well as exogenous noxious substances, *e.g.* infectious, toxic, or allergic (perivascular round cell infiltration), eosinophilia in the case reported by *Zetterholm* (1946). Muscle tissue may only be able to react to noxious substances with the stereotyped primitive reaction: round cell infiltration and degeneration. The proximal localisation in the muscles, compared with the cases which clinically have a strong resemblance to progressive muscular dystrophy, and the change in the muscle biopsy findings in cases 5 and 6 from polymyositis with muscular dystrophy of peripheral origin to the picture of clear-cut muscular dystrophy without round cell infiltration suggest that some non-hereditary cases of progressive muscular dystrophy, at any rate those with an atypical course, might begin as myositis.

Electromyography also shows a resemblance between polymyositis and non-hereditary cases of progressive muscular dystrophy.

Differential diagnosis.

The possibility of a myositis of specific origin: trichiniasis, tuberculosis, and Boeck's disease must always be considered. We think that these conditions may be excluded in our cases.

Treatment.

Case 1 was given large doses of penicillin; during treatment there was an acute exacerbation of the myositis in the strained muscles and the myocardium, and the patient died from acute myocarditis, which for some time had given alternating bundle branch block with Adams-

Stokes' attacks. Case no. 2 was first treated with penicillin; the first injections were followed by a rise in temperature to 41° ; after an interval small doses, and subsequently large doses were tolerated and had some effect.

Cases 2, 3, 4, and 5 were treated with streptomycin twice a day in two series of two weeks. In case 2 no definite effect was noticed. In case 4 the treatment had a very favourable effect as the pain, atrophy, and pareses remaining after penicillin treatment disappeared, and the sedimentation rate fell to normal. In case 5 also the pains subsided and the microscopic changes disappeared almost completely.

CONCLUSION

From the above it seems justifiable to draw the conclusion that streptomycin has some effect in some cases of chronic polymyositis, while penicillin appears in one—perhaps in two—cases to have activated the muscular inflammation.

In case 6, prostigmine had some effect. From this, however, it is not justifiable to conclude that it was a case of myasthenia gravis, as the effect of prostigmine is not necessarily specific for this disease.

SUMMARY

The authors report six cases of polymyositis verified by muscle biopsy. In three cases the lesion had a marked clinical resemblance to progressive muscular dystrophy, but in two of these muscular pain and tenderness were unusually marked; in two other patients spontaneous pain in the proximal muscles was the most conspicuous clinical sign, one case was atypical—clinically it was more like myasthenia gravis.

The etiology is still obscure. Most likely the condition represents a rather stereotyped and primitive reaction on the part of the muscle tissue to different unknown noxious substances.

Penicillin and streptomycin have been tried, and it appears that streptomycin has a therapeutic effect in some cases.

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HIGH BLOOD PRESSURE AFTER CONCUSSION

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Concussion in the acute stage was widely studied in animal experiment (Duret, Kocher-Filehne, Polis, Denny-Brown and Ritchie-Russell etc.) and also from clinical and pathological standpoint; but the chronic stage was relatively neglected. Experimental work on the latter is, to my knowledge, non existent. Pathological findings are scanty (Friedmann, etc.) and the clinical signs, especially the post-concussional headache and giddiness, are unexplained: Their mechanism is unknown; their objective assessment is impossible. No criterion is known by which a genuine case of postconcussional syndrome could be discriminated from that of a malingerer or a hysteric. Furthermore, an important sign, the postconcussional hypertension was either overlooked or its significance not appreciated.

During the last few years I have had the opportunity of studying over 300 cases of postconcussional syndrome. Unfortunately some of the records are not available so that only 81 cases will be analysed; but the rest were studied previously and they fully confirmed the results obtained from the 81 cases: 83 % of these had a blood pressure higher than the standard corresponding to their age. 40 of the 81 cases were pensioners seen on behalf of the Ministry of Pensions, and their blood pressure measurements were so unequivocal that they convinced me that hypertension is not only a fairly frequent but also a permanent, and therefore important sign of the postconcussional syndrome.

Method. The blood pressure was taken, in the hospital cases, in the morning after a night's rest in the recumbent position,—in the pensioners after a rest of 1-2 hours—with a Baumanometer, using the auscultatory method. The diastolic pressure was read at the point when the blowing sound disappeared completely. The urine was examined in all cases to exclude kidney affections.

Material. The patients were all either active or demobilised soldiers of good or medium physique and, apart from their head injury, generally healthy. The average age of the patients (non-pensioners) was 25, that of the pensioners who were all seen at boards, 33.6. The oldest of the first group was 39, that of the second group 49. The youngest of the first group was 19, that of the second 20. The pensioners were selected from a long series of surgical cases if they were found to have sustained concussion, irrespective of whether this was the pensionable disability or not. No concussion case was excluded from the latter group. The inn-patient group includes only cases of more serious nature who recovered from their acute injury but kept complaining of headache, giddiness and other sequelae. Acute cases do not appear in either group.

Standard arterial blood pressure. Robinson and Bruce reported on the basis of 11,000 persons studied, that the normal range of blood pressure is between 90 and 120 mm Hg in the systolic and between 60 and 80 in the diastolic phase. Rautmann found, on examination of 562 German young healthy men of average age of 23.7, that the normal range of pressure varied between 105 and 125 mm Hg. The standard figures given by Rogers and Hunter (based on Halls Dally, Symonds and Mackenzie) are at the age of 15: 110/70 mm, at 20: 122/80 mm, at 25: 124/81 mm, at 30: 126/82 mm, at 35: 127/83 mm, at 40: 128/84 mm, at 45: 129/85 mm Hg. We are thus on safe ground in taking 130 mm as being the limit of the normal pressure, since our average age for the 2 groups was 25 and 33.6 and the oldest man of the in-patients was 39. One man only, in the pensioner's group exceeded 45, he was 49.

RESULTS

Details of the 81 cases are given in *Table I*.

Out of these the systolic blood pressure was:

130-140 mm Hg	in 12 (1)	cases, with an average age of 26.1
140-150	" " " 12 (5)	" " " " " " 25.6
150-160	" " " 21 (13)	" " " " " " 30
160-170	" " " 11 (7)	" " " " " " 29.6
170-180	" " " 7 (5)	" " " " " " 32.6
180-190	" " " 4 (4)	" " " " " " 39.7

The figures in brackets signify the pensioners, included in the preceding figure.

Thus 83 % of all cases had a systolic pressure higher than 130 mm Hg. The diastolic pressure increased proportionately with the systolic pressure: while the average systolic pressure was 146.5, the diastolic was 91.7 mm.

I am unable to state how soon after injury the hypertension develops because the cases under consideration were not seen in the acute stage in which, as a rule, no hypertension exists. The shortest interval between injury and observation in my series was 2 months. It was also impossible to follow up the cases for a longer period; nevertheless, it became evident that hypertension caused by concussion is, in most cases, of long duration, most probably of permanent nature: Out of 71 cases in which the dates were known, 18 (0) were seen less than one year, 7 (2) between 1 and 3 years, 24 (20) between 3 and 5 years, and 22 (18) more than 5 years after injury. (The figures in brackets are those of the pensioners). It was also striking that amongst the pensioners the postconcussional hypertension was even more prevalent than amongst the in-patients, though the interval between their accident and examination was, on the average 4.5 years. The slightly higher blood pressures shown by the pensioners may be due, to some extent, to the different conditions and milieu in which the examination took place.

In addition to their concussion, 3 men suffered from epilepsy, 6 had a fractured skull. 3 of the latter 6 had a lower pressure than the average, confirming the experience that a closed skull is conducive to the development of concussion and its sequelae.

Attention was paid to the severity of symptoms in their relation to blood pressure. It is naturally difficult to assess quantitatively subjective sensations, especially in soldiers and pensioners who are obviously interested in exaggerating their complaints. Nevertheless the impression was formed that the complaints were, as a rule, in direct proportion to the increased blood pressure. Only 5 men were free from headache and giddiness, who had a systolic pressure above 130 mm Hg. The majority of those who had a normal blood pressure had no headache or giddiness; those who had were mostly hyper-reactors, as will be seen later.

The duration of amnesia following injury—which is recognised as a fair indicator of the severity of concussion—was recorded in only 59 cases. No constant relation between this factor and blood pressure could be established.

Several men had a very labile vascular system: blood pressure readings at different times showed greater variations than those taken in normal individuals. Peripheral angiospasm was also observed

in some patients. The question arose whether this lability of the vascular system could not be detected and utilised in those who, at rest, showed normal blood pressure. A functional test, the CO₂-inhalation test was therefore tried and proved successful.

CO₂-INHALATION TEST

This test is considered to be the most sensitive for detecting the irritability of the vasomotor centres (Jerusalem and Starling etc.). The application of the test for the postconcussional hypertensives appeared promising since it was found (Raab) that essential hypertensives reacted on CO₂-inhalation with a much higher increase of pressure (30-60 mm Hg) than did normal individuals. Raab gave the blood pressure increases for normal persons of different age groups as below:

Age	Initial Bp.	Average Bp. increase
20-25	109	+ '6
25-30	103	+ 10
30-35	106	+ 12
35-40	108	+ 20

RESULTS

The CO₂ test was applied in 33 cases of true or suspected postconcussional headache and in 6 cases of headache of other etiology—not included in Table I—. The test more than fulfilled my expectations: Out of 33 cases 27 had an increase of the systolic pressure by 10-20 mm, 17 cases by 20-30 mm, 9 cases by 30-40 mm, and 6 cases by 40-50 mm Hg. Altogether 26 men out of 33 had a higher pressure increase than the averages given in the table of Raab. Thus 78 % of the 33 men were hyperreactors.

This figure is even more significant if one considers that one of the 7 normal reactors was a man with a gun shot wound of the brain, and another was suspected to be a malingerer. Furthermore, all 6 non-postconcussional cases had a pressure increase of only 10 mm or less. One was a case of sun stroke (5/10 mm), 2 of migraine (10/-5 and 8/8 mm), one had an old meningitis (4/4 mm), one hysteria (5/6 mm). The upper figure indicates the increase of the systolic, the lower that of the diastolic pressure. All the results of the CO₂ test are given in Table I.

The blood pressure curves of postconcussional headache cases, in relation to CO₂ inhalation are so characteristic that, after some

experience, one may, without knowing the history of the case, judge with fair accuracy whether it is a genuine one or not. No constant relation between age and increase of pressure could be established. This question arose from the observation (Raab) that older people react on CO₂ inhalation with bigger increase than do young people. Nor does a constant relation seem to exist between initial blood pressure and the pressure increase. In 2 cases, however, with a high initial pressure the increase was below the average: 0/10 mm on the initial pressure of 150/90 mm, and 5/8 mm on 160/90 mm. The implication of this finding will be discussed later.

From the 9 cases whose blood pressure was found to be below 130 mm, 8 were submitted to the CO₂ test; of these 6 were found to be hyperreactors. Thus, *out of a total of 81 cases 73 had either hypertension or proved to be hyperreactors.* (One of the 4 negative cases was not submitted to the CO₂ test). It appears that a case which does not fall into one of the two groups may well be considered suspicious of not being a severe case of postconcussional syndrome.

The hyperventilation test of Raab which consists of comparing the blood pressure before and after deep breathing for 15 minutes, was not applied. In essential hypertensives the blood pressure was found to fall by up to 80 mm Hg. The diathermy of the brain stem will be discussed later. It is to be expected that both tests will yield similar results in postconcussional hypertensives as they did in the essential type.

LITERATURE

a) *Neurogenic hypertension.* The central neurogenic etiology of the essential hypertension was first suggested by Pal and and supported by Kahler. It was contested for a long time until clinical and experimental evidence made it acceptable. From a vast literature only a few publications will be mentioned: Dixon and Heller produced permanent hypertension in animals by injecting kaolin into the cisterna cerebello-spinalis. Raab produced increased blood pressure in decerebrated cats by reducing the oxygen supply and by perfusing the brain stem with blood containing lactic acid. He concluded that the cause of hypertension is an ischaemia of the medulla oblongata, associated with local acidosis. In logical pursuit of this idea he, and independently László and Weisel applied diathermy to the brain stem in order to produce local hyperaemia. This procedure, while having no effect on normal individuals, reduced the blood pressure of hypertensives on the average by 31 mm Hg, confirming that the blood pressure can be reduced by improved oxygenation of the brain stem. Raab

TABLE I

A) *In-patients.*

No.	Age	Bl. pr.	Pressure incr. CO ₂	Time since concussion	Unconscious for:	Symptoms - Remarks
1.	20	170/110	20/-7	8 M		h. a., g. +++
2.		170/110	20/20	6 M	few hours	h. a., g. +++
3.	18	165/100	15/15	2½ Y	2½ h	h. a., g. +++
4.	30	165/80	—	6 M	1 d	Fract. skull
5.	23	162/88	25/4	2 M	few minutes	h. a., g. +++
6.	22	160/90	5/8	8 M	3 d	h. a., g. +++
7.	21	155/105	10/4			
8.	24	154/76	—	4 Y	½ h	h. a., g. +++
9.	21	152/100	14/36	7 M	4 d	h. a., g. +++
10.	24	152/90	15/25			h. a., g. +++
11.	21	152/78	20/18			h. a. +++ Epilepsy ?
12.	26	150/110	30/30	6 M		h. a. +++
13.		150/98	—	1½ Y	25 d	h. a. +++ g. ++
14.		150/90	0/10	2½ Y	2 d	g. ++
15.	28	144/96	18/20	2½ M	few minutes	h. a. ++
16.	21	144/65	—	½ Y	½ h	h. a. + Fract. skull
17.	22	140/100	15/4	3 Y	4 d	h. a., g. +++
18.	18	140/100	40/16		dazed	h. a. ++
19.	27	140/100	8/4			Gun shot wound of brain
20.	22	140/95	45/25	1 Y	5 d	h. a., g. +++
21.	23	140/80	40/?			h. a. ++
22.	33	138/96	—	4 M	—	h. a. ++ g. ++
23.	23	136/84	25/15	7 Y	few minutes	Lability of bl. pr.
24.	21	135/110	10/5	8 M	14 d	
25.		135/60	12/5			Unilateral h. a.
26.	38	132/86	—	½ Y	few h	h. a. +++ g. +++
27.	25	130/95	30/15			h. a. +++ g. +++
28.	26	130/90	20/15	4 Y	½ h	Fract. base
29.	21	130/84	50/30	5 Y	?	h. a. +++
30.	19	130/88	—	7 Y	1 h	h. a. ++ Migrain ?
31.	25	130/80	2/0	5 M	?	h. a. ++
32.	22	130/80	4/-10	6 and 1 Y	1 h and 1 h	h. a. ?? Malingerer ?
33.	28	126/96	—	History uncertain		h. a. +++ g. +++
34.	30	125/75	30/15	Several falls with fits		Epilepsy ?
35.	25	125/95	30/20	6 Y and 3 M	few minutes	h. a. ++ g. ++
36.	37	125/88	25/22	Several injuries with fits		Epilepsy
37.		120/70	18/-12	3 M	few minutes	h. a. ++ g. ++
38.	20	120/65	6/-4	4 M	„	h. a. ++
39.		118/80	44/20			h. a. ++
40.	39	104/80	20/26	14 M	2½ d	h. a. +++ g. +++
41.		90/50	10/6	5 M		Unilateral h. a.

Bl. pr.: blood pressure; Y: year; M: month; d: day; h: hour; h.a.: headache; g: giddiness.

B) Pensioners.

No.	Age	Bl. pr.	Time since concussion	Unconscious for:	Symptoms - Remarks
1.	38	190/110	8 Y	2 d	h. a. +++ g. + After breathing for 13' Bp. decreased by 20/5 mm.
2.	49	190/115	8 Y	12 h	h. a. ++ g. + Bp. in 1946: 180/110 mm.
3.	32	190/110	4 Y		h. a. +++ g. +++ Subdural haematoma
4.	40	185/125	7 Y	12 h	h. a. ++ (occas.) g. ++ femur.
5.	44	175/110	3 Y	few min.	h. a. +++ g. ++ (constant)
6.	28	170/110	4 Y		h. a. +++ g. +++ skull
7.	40	170/100	3 Y	?	Bp. on day of accident h. a. ++ g. + 135/95; 8 months ago 165/95 mm.
8.	34	170/90	4 Y	?	h. a. ++ g. ++
9.	30	170/90	3 Y	?	h. a. +++ g. ++
10.	41	165/100	3 Y	1 h	h. a. +++ g. —
11.	28	160/110	6 Y	18 d	h. a. ++ g. ++ 1 year later Bp. 130/85 mm. Fract. skull.
12.	29	160/105	5 Y	10 h	h. a. +++ g. +++ occasion. Fract. spine
13.	31	160/100	5 Y	9 h	h. a. ++ g. ++
14.	37	160/100	6 Y	6 d	h. a. ++ g. ++ Bp. 2 years ago 160/100
15.	35	160/90	3½ Y	?	h. a. +++ g. +
16.	32	160/85	4 Y	10 min.	h. a. ++ g. — Fract. vertebrae
17.	37	156/100	4 Y	15 min.	h. a. + g. ++ Fract. spine
18.	42	156/110	6 Y	1 h	h. a. ++ g. +
19.	39	156/95	4 Y	6 h	h. a. +++ g. +++
20.	35	156/90	3½ Y	1 h	h. a. ++ g. +
21.	32	150/110	4 Y	12 h	h. a. ++ (½ sided), g. + Changed personality
22.	42	150/110	6 Y	dazed	h. a. ++ g. —
23.	30	150/100	3 Y	1 h	h. a. — g. —
24.	20	150/100	5 Y	5 d	h. a. ++ g. — Fract. femur.
25.	40	150/90	4 Y	?	h. a. ++ g. —
26.	35	150/100	9 Y	?	h. a. +++ g. +++ Spasticity
27.	30	150/90	5 Y	3 min.	no complaint
28.	26	150/85	6 Y	few h	h. a. ++ g. +
29.	25	150/75	4 Y	few min.	h. a. + occasionally
30.	29	146/85	5 Y	6 h	h. a. ++ g. ++
31.	27	144/90	7 Y	few sec.	h. a. — g. — (had h. a. the first years)
32.	29	140/90	5 Y	2 d	h. a. + g. ++ + Fract. base
33.	36	140/100	6 Y	6 h	h. a. + g. — Developed Froehlich's syndrome after accid.
34.	26	140/90	2 Y	?	h. a. — g. — Fract. vertebr.
35.	35	135/90	3 Y	7 d	h. a. — g. After accident Bp. 145/90
36.	30	125/80	3 Y	3 d	h. a. — g. — Bp. after accident 150/108
37.	31	124/80	3 Y	10 d	h. a. ++ g. +++
38.	30	124/70	3 Y	3 d	h. a. — g. — Bp. in 1945: 150/108 mm.
39.	26	120/70	6 Y	3 d	h. a. ++
40.	45	120/70	3 Y	½ h	h. a. — g. —

found also that the O-utilisation from equal volumes of blood passing through the brain substance is 25 % higher in hypertensives than in normal individuals. This is a compensation for a diminished blood supply.

Amongst pathological findings those of Bordley and Baker are of interest: they described that the blood vessels of the medulla oblongata are sclerotic in hypertensive people. Nordmann and Müller reported on a man of 22 who, during an attack of infantile paralysis, developed increasing asphyxia and hypertension. At p.m. infiltrations were found in the anterior horns of the spinal cord and further in the respiratory centre localised in the formatio reticularis grisea of the medulla oblongata. Only one other area was similarly affected, namely the substantia reticularis grisea, from the level of the facial nucleus down to the nucleus of the glossopharyngeal nerve. The authors considered the latter area to be the vasomotor regulatory centre.

b) **Postconcussional hypertension.** The literature on this subjects is very scanty; recent monographs on head injuries like that by Brock (1940) do not even mention hypertension as a sequel of concussion. Only a few *acute* cases were reported: Weissmann's case concerns a man of 43 who had normal blood pressure before his accident. 3 months after being hit by a heavy ball on his occiput and concussed, he was found to have a blood pressure of 235/140 mm Hg and complained of severe headache. His CSF-pressure and kidney function were normal; his heart was not enlarged.

Beigelböck's man was 35; he developed immediately after his fall on his occiput a pressure of 260/60 mm, whereas $\frac{1}{2}$ year before his pressure was normal. A hypothalamic lesion was suspected. Raab's woman of 45 was unconscious for 5 $\frac{1}{2}$ hours after a fall on her head. The following day her Bp was 115/70 mm Hg. The next 6 days her temperature was irregular, rising to 41 C°, and her pulse varied between 120 and 160. From the tenth day the blood pressure rose to 200/120 mm, in attacks lasting for hours and running parallel with the rising temperature; both returned to normal at intervals. Raab attributed the attacks of hypertension and hyperpyrexia to haemorrhages in the hypothalamus.

As to hypertension in *chronic* postconcussional cases, Marburg noticed that concussion in young people is followed sometimes by a pressure of 140-150 mm Hg, and that in 55 % of the late stages a hypertension of the retinal arteries is present. The latter observation was confirmed also by Tirelli. Raab and Knud Winkler deny the postconcussional hypertension to be common. Zetterholm recorded

hypertension in 7 of his chronic cases examined from a different angle. Nothing is known, as far as I could find, about the further course, and therapy of these cases. How is it that an important sign like hypertension could escape attention? Most probably the decreased blood pressure caused by the shock in the acute stage masks temporarily the rise. I do not know how long this period of overlapping of the two reactions lasts, but it is likely that the hypertension becomes manifest several weeks after the injury when the patient usually left hospital.

In the light of my clinical observations the experiments of Polis and Denny-Brown and Ritchie-Russell are of great interest, though these authors studied the effect of concussion only in the acute stage and in animals. Polis showed that concussion in rabbits, cats and dogs was consistently accompanied by arrested respiration and a very considerable rise of blood pressure (e.g. from 161 to 315 or from 98 to 183 mm in dogs). He speaks of a "desequilibration des centres du bulbe". This was confirmed by Denny-Brown and Ritchie-Russell and previously by Duret and Kocher and Filehne. Duret considered the anatomical changes of the medulla obl. to be fundamental in concussion. An initial rise of blood pressure is followed by a prolonged fall and ends in a gradual recovery or steep failure. In concussion of moderate degree this second phase may be characterised by a raised resting level for several minutes "as if the vasomotor centre continued to be stimulated by concussion". The final failure is not regarded as being due to a paralysis of the vasomotor centre for it is accompanied by intense peripheral vasoconstriction. This constriction is due to direct stimulation of the vasomotor centre in the medulla.

DISCUSSION

The first question is whether hypertension is the direct result of concussion or whether the postconcussional syndrome is more likely to develop in hypertensive and potentially hypertensive individuals. There is ample evidence that some of the postconcussional hypertensives had a normal blood pressure before injury and that hypertension was direct and immediate sequel to concussion. The acute cases of Raab and Beiglböck are such examples. There was no evidence in any of my cases of complaints suggesting hypertension before injury. This, however, does not exclude the possibility that postconcussional hypertension develops preferably in people who are in the hypertensive state. This possibility is rendered improbable by the

fact that the proportion of hypertensives amongst concussed individuals is much higher than the proportion of prehypertensives to normal people. It is noteworthy that my cases never reached a pressure above 190 mm Hg. If the hypertensives were the predisposed victims of postconcussional syndrome, one should expect that people with the highest pressure would be primarily affected. That apparently is not so.

The vasomotor centres are localised in the medulla oblongata and hypothalamus. On the other hand the medulla is known to be one of the localisations in which minute haemorrhages are likely to occur (Duret). Berner considers haemorrhages of the brain stem important in the genesis of concussion. They were confirmed also by Denny-Brown and Ritchie-Russell. It is well conceivable that these haemorrhages interfere with the function of the medulla and thus cause pathological blood pressures. They are evidently anatomical manifestations of an interrupted blood supply. The inadequate oxygenation of the brain stem with consequent accumulation of lactic acid leads to an increased blood pressure, (Raab).

The experiments of Polis and Denny-Brown and Ritchie-Russell demonstrate that postconcussive hypertension in animals is not only conceivable, but is the rule, at least in the acute phase. The later developments in animals are unknown. In short, experimental as well as clinical evidence strongly support the assumption that *hypertension is the direct result of concussion, caused by stimulation of the vasomotor centre.*

The subjective symptoms of the two conditions, the hypertensive state and the postconcussional syndrome are very similar. Both are characterised by severe, persistent headache, giddiness and lack of concentration; in both, these symptoms become accentuated on exertion. The question then arises whether the symptoms of the postconcussional syndrome are not wholly or partly due to the increased blood pressure. One has to admit there are some cases of postconcussional syndrome with severe headache etc. without hypertension and vice versa; but these are very few and these few may be caused by other complications (meningeal adhesions etc.). But, it is most likely that these people, though apparently normal at rest, do get high blood pressure on exertion. We have seen that most of them do so after inhaling CO₂. From the standpoint of oxygenation of the vasomotor centre and accumulation of lactic acid the two processes, exertion and CO₂ inhalation, are similar in their end effect.

Why does postconcussional hypertension not reach a higher degree than 180-190 mm Hg? It is most likely that many cases of acute con-

cussion in which the anatomical changes of the medulla are severe do not survive because of the proximity of the vasomotor to the respiratory centre. We saw this in the case of Nordmann and Müller in which the joint affection of the two centres ended fatally. The joint affection of these two centres was pointed out also by Denny-Brown and Ritchie-Russell. Only people with slight lesions of the medulla have the chance of surviving; the acute cases of Raab, Beiglböck and Weissmann, which had a blood pressure of around 200 mm Hg are not the rule but exceptions.

It is at present impossible to express an opinion on the ultimate fate of postconcussional hypertensives. If they follow the course of the "hyperreactors", which they undoubtedly are, their prospect is poor. According to Golding 38 % of the hyperreactors develop hypertension within 6 years after their first detection. This pessimistic view is rather confirmed by the high proportion of hypertensives amongst the pensioners examined and also by the higher range of their blood pressure. There was a much longer lapse of time between their injury and their examination, compared with the soldiers, yet their blood pressures were considerably higher. There was definitely no downward tendency of their pressures detectable.

We have seen that the postconcussional hypertensives were not always hyperreactors, some were even hypo-reactors. From this fact it appears that postconcussional hypertension is caused, as is the essential type, partly by an arteriolar spasm of the vasomotor centre, partly by permanent physical vascular obstruction. Vascular spasm will react to CO₂ inhalation by dilatation, but blocked vessels (atherosclerosis, thrombosis) are incapable of dilating. This might be the reason why 2 cases of my series with high initial pressure showed the least pressure increase. Such cases might have a poor prognosis if my explanation is correct.

The practical significance of drawing attention to the prevalence of postconcussional hypertension will be felt in several directions: Diagnostically, it will be possible in a high proportion of cases to detect whether the case is a genuine one or not. If a young patient's blood pressure should be found to be constantly above 130 mm Hg, or though apparently normal at rest, should react to CO₂ inhalation with a rise of blood pressure of more than 8-10 mm Hg, it is very likely that such a case is a genuine one, provided that other causes of hypertension are excluded. The detection of genuine cases will be of advantage especially to insurance companies and all companies dealing with accident cases.

Another dysfunction of the brain stem, following concussion was

described recently by Stähli, Schürch, Becker and Domanik (1947). It manifests itself in a diminished sugar tolerance, and appears during the first days after injury, but may persist in more severe cases for weeks. The authors ascribe a diagnostic and prognostic value to the sugar tolerance test. The abnormal sugar tolerance is probably caused by a hypothalamic lesion which might be partly responsible also for the postconcussional hypertension. However, while the latter is of a permanent nature, the sugar tolerance decrease appears to be transitory as far as one can judge from the reports so far available.

THERAPY

If my assumption is correct that in a high proportion of cases of postconcussional syndrome the headache and giddiness are caused by hypertension, then their treatment ought to be conducted on the same lines as that of essential hypertensive disease. Unfortunately the therapeutic possibilities of the latter are, at present, very limited; still, eventual progress in its treatment will also benefit postconcussional hypertension. Potassium thio-cyanate has not been tried in these cases, nor has László and Weisel's diathermy of the brain stem; they may both be found to be beneficial. The latter should, however, not be attempted earlier than 2-3 weeks after the acute stage to avoid danger of renewed haemorrhage.

In many diseases caused by physical or functional vascular impairment a vicious circle develops which leads to an eventual increase of pathological conditions. An early break of the circle, by improving the blood supply and decreasing the excitability of the centre concerned—in our case the vasomotor centre—may result in a permanent improvement. A trial of the brain stem diathermy after concussion appears, therefore, very well worth while.

A drug which, as far as I know, has not been tried out in cerebral vascular affections of spastic nature, is Priscol (Ciba). It is a potent vasodilator, the effect of which lasts for about 6 hours, in contrast to other vasodilators like histamine and acetylcholine. I tested its effect on cerebral blood vessels by capillary microscopy through a window in the skull of cats, and found it to be a powerful vasodilator. I have not tested the duration of its action in the brain, nor have I any personal experience of its effect on postconcussional headache. The beneficial effect of Priscol, if any, after concussion might be the breaking of the vicious circle above mentioned.

Sympathectomy of the cervical ganglia may have a similar effect of longer duration. The CO₂ test might be useful in the selection of

the right type of case for sympathectomy: If a patient's blood pressure, after CO₂ inhalation does not rise by more than 10-15 mm Hg it can be taken that his cerebral blood vessels are no longer capable of dilating. In such case a permanent damage of the blood vessels can be assumed to be the underlying cause of the symptoms, and it is most unlikely that such a patient will benefit from sympathectomy.

If useful conclusions can be drawn from clinical and pathological observation of essential hypertensives, as to the etiology and therapy of postconcussional cases, the same may apply in the reverse: The clinical observations made in postconcussional hypertensives and the pathological findings in experimental animals may help to solve some of the obscure problems of hypertensive disease. My own observations may convince the few doubters of the existence of a central neurogenic hypertension.

RESUMÉ

Over 300 cases of postconcussional syndrome were examined and 81 were analysed in more detail: 83 % of the latter had a blood pressure higher than the standard of their age.

78 % of 33 men submitted to the CO₂ test proved to be hyperreactors; these included 6 men, out of 8 tested, who had a blood pressure below 130 mm Hg at rest.

Thus, out of a total of 81 cases 73 were either hypertensives or hyperreactors. These figures may be so high because they were obtained from a selected material comprising more serious cases. It is suggested that the postconcussional symptoms (headache, giddiness etc.) are, at least partly, caused by hypertension.

The diagnostic and prognostic significance of postconcussional hypertension are stressed.

As therapeutic measures Potass. thio-cyanate, brain-stem diathermy, Priscol and cervical sympathectomy are discussed. Sympathectomy is disadvised in cases which do not respond with a blood pressure increase of over 10-15 mm Hg to CO₂ inhalation.

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REMARKS ON ELECTROENCEPHALOGRAPHY IN CEREBRAL ABSCESS

By

ÖYSTEIN FARBROT

INTRODUCTION

Since the new chemotherapeutic agents became common in treatment of cerebral abscess the prognosis of this condition has improved considerably. Early and accurate diagnosis of the illness has therefore acquired increased importance.

In the present paper the value of electroencephalography (EEG) in cerebral abscess will be dealt with, illustrated by a few cases. In most of the cases repeated EEG's were performed during the convalescent period and the findings will be discussed.

Reports in literature on EEG in cerebral abscess seem to be fairly rare. In 1940 *Grey Walter* (6) published a report on 7 cases of cerebral abscess examined by EEG. He states that EEG is of great value for the localization for cerebral abscess. It is mentioned that EEG should be performed when intracranial complications of oto-rhinological diseases are suspected. It is further emphasized that EEG examination causes no deterioration of the patient's condition, even if it is poor.

In 1942 *R. S. Schwab* and *R. Carter* (8) recorded 15 cases of cerebral abscess. Dysrhythmia was found in 14 cases. The fifteenth case was a cerebellar abscess showing a normal record. The authors conclude from this series that EEG is very valuable for the localization of cerebral abscess and are of opinion that a normal EEG is good evidence against brain abscess.

In 1944 *W. A. Cobb* (3) published a report on 125 cases of intracranial neoplasm. In this series there was a group of 5 cerebral abscesses, which all showed electrical cerebral dysrhythmia and in 4 of which correct localization was obtained. The author remarks that cerebral abscesses affect the EEG in a similar manner to tumours. On account of their greater acuity, however, they tend to show more intense and slower electrical activity than the tumours.

Denis Williams (7) in a survey on the significance of the normal EEG (1948) states that if the EEG is normal, it cannot be a case of recent abscess.

METHOD

The EEG examinations have been performed by a 3-channel, Kaiser electroencephalograph with ink-writing recording system. Its construction was dealt with by Buchthal and Kaiser in *Acta psychiat. et neurol.* 1943: 18: 389-409, to which article readers are referred. A localization technique as indicated by Gibbs and Gibbs in the *Atlas of Electroencephalography* has been used. In addition to that an electrode has as a matter of routine been placed on each ear lobe and used as a reference in "unipolar" leads. The 8 electrodes placed over the left hemisphere have been combined with the ear lobe electrode on the left side and vice versa. To get some impression of the electrical cerebral activity coming from the ear lobe electrodes themselves short tracings with the combination "left ear/right ear" have been made. On account of the patient's poor condition two records were made with only three electrodes on each half of the scalp and one on each ear lobe.—Recording time was more than 20 minutes per examination. An amplification was applied which gave a deflection of the pens of c. 6 mm corresponding to 50 microvolts. Paper speed was 3 cm per second. No filters were used on the amplifiers.

MATERIAL

From October 1948 to October 1949 seven cases diagnosed as cerebral abscess were examined electroencephalographically in the neurological department of the Rikshospital. These 7 patients were totally recorded 25 times and the above-mentioned combined bipolar and "unipolar" localization technique was used in 23 of these records. In the two remaining cases a simpler method was used.

In 4 of the 7 cases cavities containing pus were found, in 3 by surgical intervention, in 1 by post mortem examination. These 4 cases will in the subsequent communication constitute group I.—The remaining 3 cases constitute group II. Here the diagnosis of cerebral abscess is not definitely proved, but anamnesis, clinical findings, spinal fluid and blood examinations combined with the results of repeated EEG recordings with constant focal findings make such a diagnosis very probable. In this second group signs of expanding lesion were found by cerebral angiography in one case. Another patient of group II

died of acute meningitis 6½ months after he had left the hospital the first time. Post mortem examination revealed atrophy and destruction of the right frontal lobe, indicating a relatively old lesion. (Below this patient is mentioned as case 6).

CASE REPORTS

Short descriptions of the different cases will be given below. Patients in group I will be dealt with first.

Case 1: S. F., man, aged 30. (Samples of records from different EEG examinations of this patient are reproduced in fig. 1). The patient was admitted to the neurological department in a state of coma on October 22, 1948. One month before he had caught a cold but had no fever. About a fortnight later he developed a headache with maximum in the frontal region on the right side. He felt transient mental changes which he characterized as a peculiar "feeling of catastrophe". Two days after this had occurred the first time he had a convulsive fit with loss of consciousness. He was sent to a hospital and improved a little during the following days. But on October 20 the illness rapidly grew more serious. On arrival at the neurological department he was in a coma. There was a beginning papilledema on both sides. Pupils were unequal ($R < L$) and they did not react to light. Corneal reflexes could not be elicited. He had a hemiparesis on the left side, neck rigidity and positive Kernig's sign. Deep reflexes were exaggerated in the left arm and very feeble in the left leg. Abdominal reflexes were feeble on the left side. Plantar reflexes showed dorsal response on the left side. Temperature was normal. Pulse: 56, regular. Spinal puncture revealed increased pressure and 100 cells per mm^3 in one sample, 120 cells per mm^3 in another sample. Blood: 12,600 leucocytes. Sedimentation rate 29 mm/ 1 h. X-ray examination of accessory sinuses showed no certain pathological changes.

EEG on October 23 (with 6 electrodes on the scalp) showed a severe dysrhythmia which was most prominent over the right hemisphere (fig. 1 a). Percutaneous cerebral angiography immediately afterwards gave the picture of a large expanding lesion in the temporoparietal region on the right side. Puncture was performed through a burr hole, c. 50 cc. of pus aspirated and penicillin deposited in the cavity. For the following weeks the patient was treated with large doses of penicillin and sulphadiazine and improved satisfactorily.

A second EEG on November 11 (fig. 1 b) showed improvement compared with the former record, but there was still a marked temporoparietal focus. EEG on December 17 (fig. 1 c) probably showed a slight improvement since the previous recording. Cerebral angiography on the same day revealed: "Complete resolution of the expanding lesion in the right temporal region."

After the stay in the department the patient continued to use antiepileptic medication. In April 1949 he had a regular epileptic fit. EEG on May 7, 1949, revealed approximately the same picture as in the previous EEG examination. He has, however, been at work most of the time till now, nearly one year after the operation.

Case 2: K. R., girl, 14 years old. Her illness started about September 10, 1948. A fortnight later she was submitted to an operation because of a left side

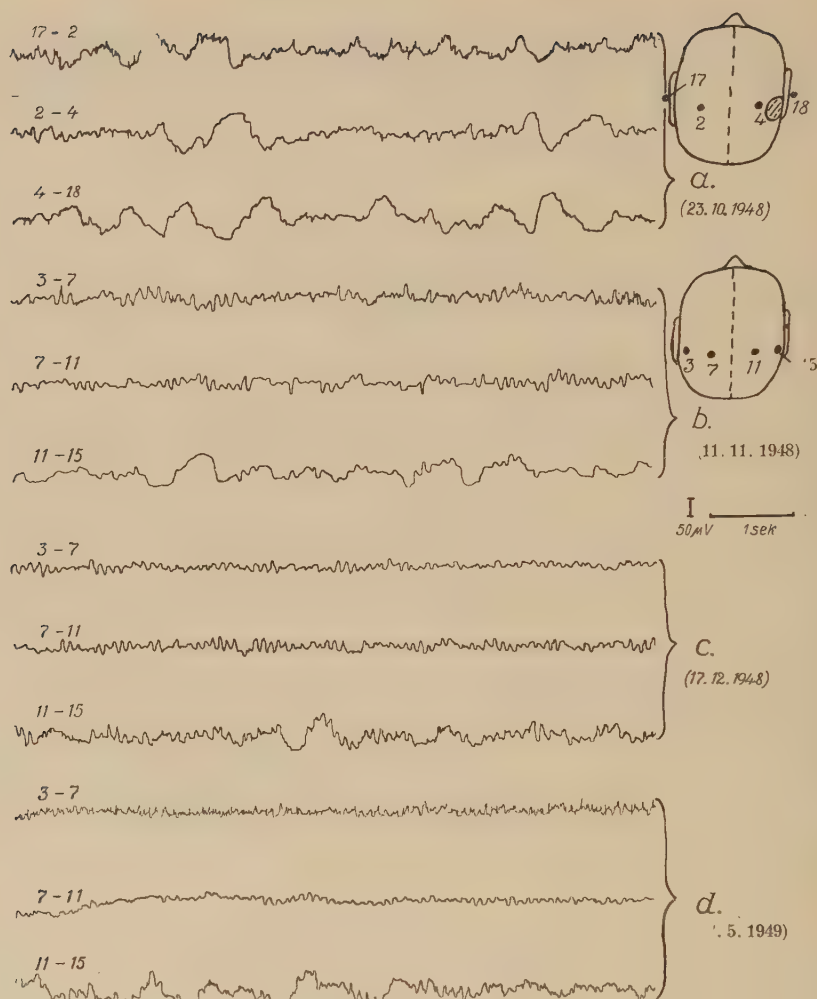


Fig. 1.

Case 1, S. F., man, aged 30.

(Seat of abscess indicated on the figure above).

sinusitis with complications. November 4 she got a headache and vomitus. Choked disks were found. Since November 10 it was estimated that intracranial complications were present and she was treated with penicillin and sulphadiazine in large doses. On December 8 the patient was admitted to the neurological department. She then revealed marked mental changes with torpor and confusion. There was bilateral papilledema and signs of lesion in the left hemisphere. Cerebral angiography revealed a considerable expanding lesion on the left side, probably parietal or frontoparietal. EEG showed a rather severe dysrhythmia with a focus in the frontoparietal region on the left side.

The patient was treated with puncture. The abscess was found in the frontoparietal region. During the following weeks treatment with penicillin and sulpha-

diazine was continued. EEG control records 1 and 7 months after the surgical intervention showed a slight improvement of the dysrhythmia. But still after 7 months a marked dysrhythmia persisted. During the puncture treatment the patient got a marked paresis of the right arm and hand. This has not hitherto improved. Considerable mental changes persisted too.

Case 3: H. D., woman, aged 31. She was admitted to the neurological department on February 13, 1949. Seven months earlier she had a series of convulsive fits with loss of consciousness. She was sent to a hospital where moderate pathological changes were found in the spinal fluid.

On admission to the neurological department she had slow cerebation and neurological signs of a lesion in the right hemisphere. An EEG showed a distinct, rather extensive focus in the right frontal region. Cerebral angiography revealed a considerable expanding lesion in the same region. Craniotomy was performed and a deep-seated abscess punctured. The following weeks the patient was treated with large doses of penicillin. Two months after the operation cerebral angiography showed a considerable improvement of the pathological features. An EEG at the same time revealed a rather slight focus in the right frontal region. Clinically the patient recovered very satisfactorily during the stay in the department, and afterwards she felt quite well till on October 2, 1949, she had an epileptic fit with convulsions on the left side. An EEG three weeks later revealed in the right frontal region a rather pronounced focus, which was supposed to be "epileptogenic" in type. Angiography showed deviation of the anterior right cerebral artery on the right and by reoperation a marked atrophy of the right frontal lobe was found.

Case 4: J. Aa., man, 24 years. This patient was admitted to the neurological department on September 24, 1948. He was then in a very poor condition, which rapidly deteriorated. EEG showed a very severe dysrhythmia with a parietofrontal focus on the left side. The patient died before angiography had been performed. Post mortem examination revealed a large abscess cavity in the parietal region, left side. Pus could also be seen in the cisterna magna.

The 3 remaining cases are considered in group II.

Case 5: L. B., man, aged 60. For ca. 20 years he had had sinusitis from time to time. On March 3, 1949, he was operated for pansinusitis. A few days later he became drowsy and had a constant headache. There was incontinence of urine and probably paresis of the left arm. During the next three weeks he recovered a little, but the headache continued. Ultimo March he became drowsy again. Neurological signs indicated a lesion in the right hemisphere. Spinal fluid showed 51 cells per mm³. The protein content was raised. The patient was admitted to the neurological department on April 6, 1949. He had slow cerebation but no confusion. Eye-grounds were normal. Neurological examination revealed moderate signs of lesion in the right hemisphere. Temperature was normal. Blood: 8,080 leucocytes. Sedimentation rate: 70 mm/1 h. Cerebral angiography showed in right frontal region a considerable expanding lesion which might well be an abscess. EEG on April 11 showed a rather severe dysrhythmia with a marked focus in the frontal region, right side. The lesion was assumed to be deep down in the rear part of the frontal region. X-ray of skull with accessory sinuses showed affection of both maxillary sinuses and probably of the frontal sinus.

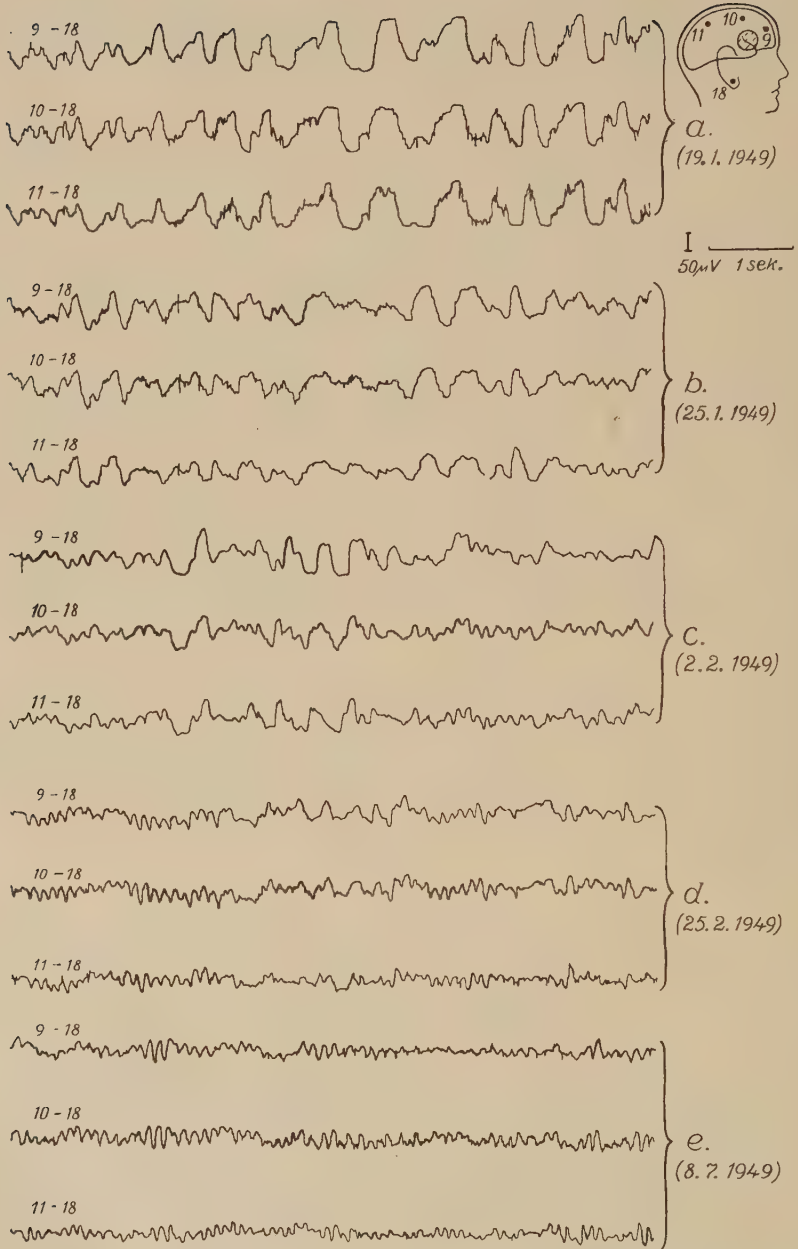


Fig. 2.

Case 6, B. J., man, aged 40.

(Seat of EEG focus indicated on the figure above).

After admittance the patient was treated with penicillin alone. EEG control one month after the first recording showed a considerable improvement of the dysrhythmia and the focus was now little pronounced. EEG's 6 and 8 weeks after admittance to this department showed further improvement. Controls with cerebral angiography the first time revealed reduction of the expounding lesion, and after two months it was concluded: "Abscess probably cured".

Case 6: B. J., man, aged 40. (Samples of different records from this patient are reproduced in fig. 2). The patient was admitted to the neurological department on January 18, 1949, in a somnolent state. Six years before he had had a skull fracture with deformation of the right frontal sinus. Primo December 1948 he began to have headaches. On January 11, 1949, he had an epileptic seizure and was sent to a hospital. The spinal fluid was then cloudy with too high pressure. It contained c. 21,000 cells per mm³, chiefly polynuclear leucocytes, and Gram-positive bacilli, estimated to be pneumococci. He had pansinusitis purulenta, neck rigidity, and neurological signs of lesion in the right hemisphere. From January 14 he was treated with large doses of penicillin. His right frontal sinus was operated upon. The dura was inspected in a small area without any special pathological findings being made. During the following days the patient had generalized epileptic seizures. Blood examination on January 17 revealed 20,400 leucocytes. Sedimentation rate: 123 mm/1 h. Neurological examination on January 17 revealed findings corresponding to a lesion in the right hemisphere. In the neurological department treatment with penicillin was continued till January 31. The patient improved considerably during this time. Cerebral angiography on February 19 revealed negative findings. EEG on January 19 showed a considerable dysrhythmia with a focus in the frontotemporal region on the right side (fig. 2 a). Control recordings on January 25, February 2, and 25 showed speedy and considerable improvement in the electroencephalographic picture (figs. 2 b, c, and d). The patient left the department on March 3, and seemed to be cured. An EEG control record taken on July 8, 1949, showed an almost normal picture. In the meantime the patient had felt quite well and had been at work since soon after he left the hospital. About September 16, 1949, the patient caught a cold, but was at work the following week. Then he suddenly got drowsy. Next morning he was admitted to the oto-rhino-laryngological department of the Rikshospital, where he died of meningitis the following day. Spinal puncture had shown raised pressure and 30,000 cells per mm³. Post mortem examination revealed meningitic changes and there was atrophy of the right frontal lobe, indicating a somewhat older affection. After the first EEG examination of this patient a focus was indicated which seems to have been somewhat posterior to the site of this lesion. Later examinations, however, revealed rather good correlation.

Case 7: T. S., girl, 8 years old. (Samples of tracings from different records of this patient are reproduced in fig. 3). Primo April 1949 she caught a cold, but this was over when on April 29 she got some nausea and vomitus. On May 2 she felt pains in left side of the front. Since May 7 she was drowsy and had paroxysms of pain in the head. There was a dysphasia. She was sent to a hospital on May 10. She then presented slow cerebation and neck rigidity. Temperature was normal. Spinal puncture showed slightly increased pressure and the spinal fluid contained 1,100 cells per mm³ and Gram-positive cocci. Treatment with penicillin and sulphadiazine was started. Neurological examination on May 11 revealed choked disks,

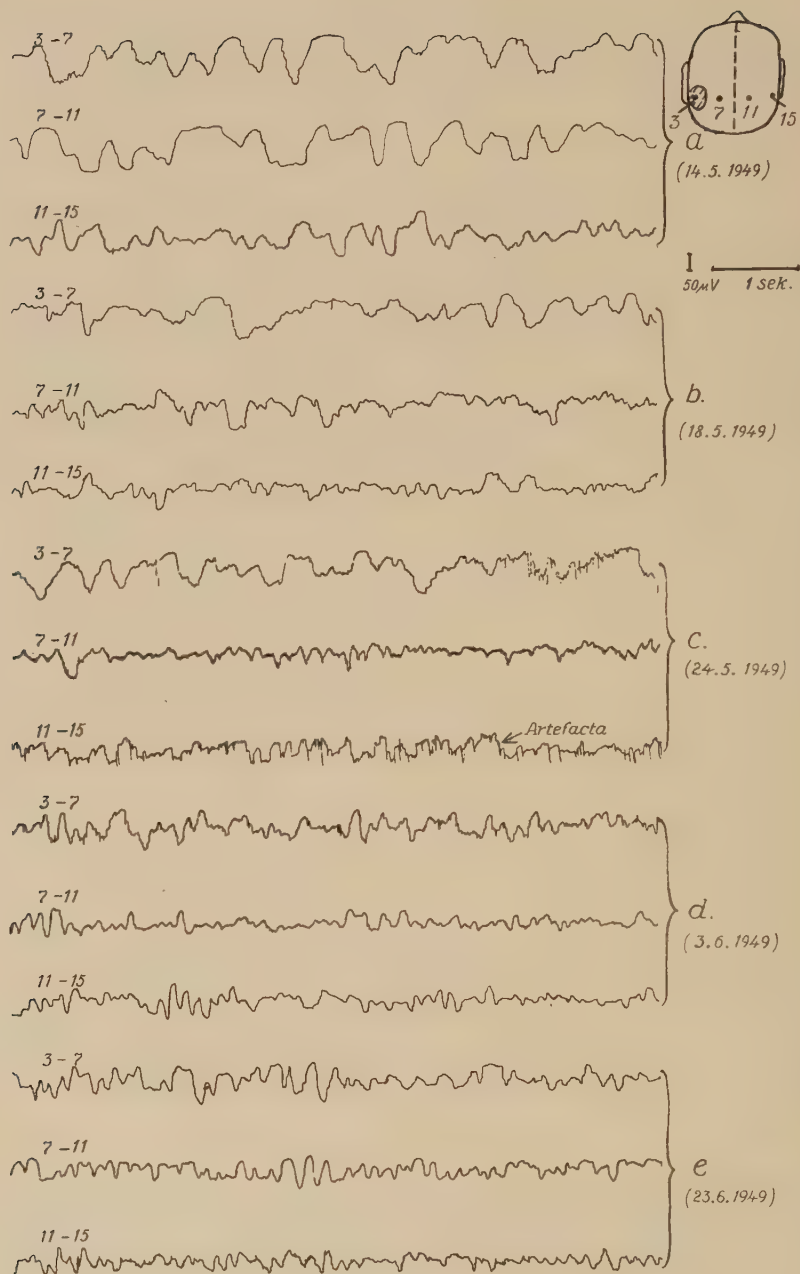


Fig. 3.

Case 7, T. S., girl, aged 8.

(Seat of EEG focus indicated on the figure above).

paresis of the left sixth nerve, jaw-deviation to the left, facial paresis on the right side and dysphasia.

On admission to the neurological department she had slow cerebation and seemed to be confused. Findings as mentioned above were made and the treatment with penicillin and sulphadiazine continued. Four days afterwards a rash occurred, which disappeared when the medication with sulphadiazine was stopped. On May 16 the patient had bilateral paresis of the sixth nerves. The papilledema was as before. The patient had a marked dysphasia.

X-ray examination of accessory sinuses showed a blurring of the left maxillary sinus. The patient was treated with penicillin till June 2, and she improved considerably. During the first days of her stay in the department the patient had a slightly raised temperature, later on she had no fever. She left the hospital on June 29 and seemed to be completely cured. By EEG examination on May 14 (fig. 3 a) a considerable dysrhythmia with temporoparietal focus on the left side was found. At the time of the second recording on May 18 the paresis of the sixth nerve had become bilateral. The EEG, however, showed a moderate improvement with a somewhat less marked focus in the same region as found by the first examination (fig. 3 b). Later recordings on May 24, June 3, and 23 (figs. 3 c, d and e) revealed a rather rapid improvement in the EEG. There was only a small remainder of the focus left at the last examination.—The patient then seemed to feel quite well. The above-mentioned neurological symptoms had almost completely disappeared.

RESULTS

In 3 of the 4 cases in which pus-filled cavities were found the EEG report indicated a sufficiently accurate localization of the lesion. In the fourth case the correct side was indicated. (Record from 6 electrodes on the scalp, the patient being in a very poor condition). Two of these cases showed a considerable dysrhythmia more than six months after the acute stage of the illness. In both of them symptoms of late complications have occurred. EEG record two months after operation revealed in one patient (case 3) a considerable improvement of the electroencephalographic picture. The clinical improvement had been very satisfactory as well. Seven months after the operation the patient, however, had an epileptic seizure with convulsions on the left side. Another EEG examination three weeks later revealed in the right frontal region a focus which was more pronounced than that in the previous record. The EEG pattern, however, was this time of a somewhat different type, and an "epileptogenic focus" suggested. Re-operation showed atrophy of the frontal lobe.

In group II all patients had a rather severe focal dysrhythmia in the first recordings of the patients. The EEG picture, however, constantly and rapidly improved, the records being almost normal at the last EEG examinations. These patients had all been treated with penicillin or penicillin-sulphadiazine alone. Clinically they all improved very

well during this treatment and two of them have hitherto shown no signs of later complications. One patient died of meningitis 6½ months after his first stay in the hospital. The meningitis was in all probability due to a new infection.

COMMENT

The dysrhythmia in acute cerebral abscess belongs to the most severe that may be seen. In the two most acute cases waves as slow as about 0.75 c/1 sec. were recorded (cases 1 and 4). The patient mentioned as case 3 had probably suffered from cerebral abscess for about 7 months before surgical intervention. Even here the dysrhythmia was pronounced, but was not of the severest type. In case 2 the dysrhythmia was of approximately the same degree as in case 3. Also here the patient's medical record and clinical findings made it probable that the abscess formation had taken place some time before the patient was admitted to the neurological department. This patient had also had penicillin-sulphadiazine therapy for a couple of days before the first record was made.—In one case of cerebral abscess examined electroencephalographically by *S. Refsum* in 1945 the patient's medical record gave reason to believe that the patient had got the abscess about 25 years before operation. Also in this case an EEG focus corresponding to the localization of the abscess was found. The dysrhythmia, however, was not so pronounced as in any of the cases mentioned above. There is reason to believe that "older" abscesses which are well incapsuled give a lower degree of dysrhythmia than do the acute forms. The author is inclined to believe that the acute abscesses produce so severe dysrhythmia that the EEG report in such cases may give some information about the nature of the focus recorded. And he feels inclined to submit that it is the rapid expansion more than the nature of the lesion, which decides the high degree of dysrhythmia.

Cerebral angiography was performed in 5 of the 7 cases. In 4 of them there was good correlation between angiographic and EEG findings. EEG and cerebral angiography sufficed for determining the focal diagnosis in 4 out of 5 cases in which angiography had been done. In the fifth case angiography had been done 5 weeks after the treatment with penicillin and sulphadiazine was started.

Two patients (cases 1 and 2) were treated with puncture and afterwards large doses of penicillin and sulphadiazine were given. During the first month the dysrhythmia decreased, but for the following about six months a marked focal dysrhythmia of approximately the same

degree persisted in both cases. In case 1 a normal angiographic picture was found two months after the acute stage of the illness. In both cases late complications have developed. In case 1 an epileptic seizure occurred five months after the acute stage of the illness. In case 2 a right-sided monoparesis and considerable mental changes persisted. The third of the patients operated upon had an epileptic seizure 7 months after the treatment.

In all patients of group II there was a constant and rather rapid improvement in the EEG at repeated examinations. At the time of the last recordings focal findings had nearly completely disappeared and the EEG become almost normal. The frequencies of the slow waves got gradually higher, the amplitudes lower, and the extension of the focus was diminished. These foci, however, had approximately the same localization as long as they could be seen in the tracings. All these patients felt quite well at the time of the last control recording, 2 to 6 months after the acute stage of the illness. Signs of late complications have not yet occurred in 2 of the cases. One patient died of acute meningitis 6½ months after the first stay in hospital. This was probably due to a new infection. In one patient (case 7) paresis of the sixth nerves increased while EEG at the same time improved (figs. 3 a and b). In this case improvement in the EEG was registered a few days after treatment with penicillin and sulphadiazine had been started. All patients in group II were treated with penicillin or penicillin-sulphadiazine only.

EEG is a method of examination which does not represent any stress on the patients. They may therefore be submitted to repeated EEG examinations without their condition deteriorating.

SUMMARY AND CONCLUSIONS

7 cases diagnosed as cerebral abscess have been examined by EEG. In 3 of them pus-filled cavities were found by operation, in 1 by post mortem examination (group I). 3 patients (group II) were treated with chemotherapy alone.

But for the patient who died shortly after admission to the hospital all the patients were examined repeatedly during the convalescent period. In all patients focal dysrhythmias were found.

The material is too small for definite conclusions to be drawn, but the author feels assured that the following statements are warranted:

- (a) EEG is of great value for a localization of cerebral abscess, partly because the dysrhythmia occurs at an early stage of the illness.

- (b) Repeated EEG's in the convalescent period are of importance for an evaluation of the treatment, and may give hints about prognosis as to late complications.
- (c) In some cases of recent abscess or incipient abscess it may possibly be an indication to try treatment with chemotherapy alone, provided repeated EEG's at frequent intervals can be carried out.
- (d) The dysrhythmia in recent abscess seems to be so severe that EEG may give some information not only about the localization, but also about the nature of the focus recorded. EEG in cases of recent abscess seems to give more severe dysrhythmias than in cases with a comparatively long history of illness, the rapidity of the expanding process here being a deciding factor.
- (e) The combination EEG-cerebral angiography in addition to the clinical examination is very useful for the exact localization of cerebral abscess.

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A STUDY OF THE POTASSIUM AND SODIUM CONTENT OF THE BLOOD SERUM IN SCHIZOPHRENIC SUBJECTS

By

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This study of the potassium and sodium content of the blood serum in schizophrenic subjects was undertaken in an endeavour to throw further light on the relationship of the adrenal glands to the schizophrenic psychosis. Before dealing with the pathogenesis of schizophrenia, I shall give a brief account of the hormonal function of the adrenal glands, especially the mode of action of the cortical hormone.

There appears to be some disagreement as to the number of hormones produced by the adrenal cortex. In *Grollman's* opinion it is only a question of one hormone, whereas *Cameron* divides the cortical hormones into 2 groups: Group 1 comprising steroids of significance to the electrolytes of the blood and the phosphorylation processes in the body and Group 2 comprising steroids of significance to the sugar metabolism as well as steroids controlling the body's mechanisms in the face of noxae.

According to this classification there should be at least 3 separate hormones, and, in addition, perhaps still another belonging to the sex hormones. The problem of the interrelationship of the adrenals and the gonads has not yet been definitely elucidated, but it is a fact that cortical insufficiency entails disturbance in sexual function in the form of testicular and ovarian atrophy. According to *Rudolf Abderhalden* the adrenals should produce certain preliminary stages of the sex hormones, a process which then should be completed in the ovaries and testes.

I shall now proceed to deal with the effects of cortin, beginning with its effect on the metabolism of water and electrolytes. Deficiency in cortin leads to a decrease in sodium and water and an increase in potassium and urea nitrogen in the blood. The disturbance in sodium and water content is considered to be partly due to failure of the kidney to re-absorb water and sodium at the same time as it re-absorbs potassium and urea in increased amounts, partly to increased extra-

vasation of sodium and water from the blood stream, simultaneously with absorption of potassium, *inter alia* in order to maintain the osmotic pressure. As the loss of sodium is relatively higher than that of chlorine, the amount of Ph in the blood stream is reduced.

Cortin is one of the hormones which influence the carbohydrate metabolism, interfering with all processes of phosphorylation which cannot take place normally without cortin. The breakdown and formation of glycogen is disturbed, and deficiency in cortin entails a reduced amount of the glycogen stored in the liver and muscles. The absorption of carbohydrates from the intestine in the phosphorylation into hexosephosphates will be arrested. The transformation of lactic acid and pyruvic acid into glucose will be arrested for the same reason. In consequence, the blood sugar will be low and the blood sugar tolerance curve flattened with delayed return to normal, if the cortin is deficient. In addition, cortin appears to accelerate the formation of glucose from fats and particularly proteins. Of course, this also contributes to reducing the blood sugar in cortin deficiency.

Lastly, the question as to whether the adrenal cortex produces a hormone acting on noxae, i.e. bacterial toxins, histamine shock, fluctuations in temperature, etc. Opinions are divided. *Hartmann, Lockwood, & Lockie* have demonstrated that adrenalectomized rats possess less resistance to the action of heat and cold than normal rats, but according to *Grollman* this should be due to a general state of weakness following adrenalectomy.

In consequence of the above-mentioned actions of the cortin, a deficiency will lead not only to reduced serum sodium, increased serum potassium and blood urea, compromised metabolism and a low blood sugar level, but also to a fall in blood pressure, a fall in temperature, a reduced basal metabolic rate, and hypertrophy of the lymphatic system. The patients are tired and debilitated, apathetic, and at times psychotic.

When perusing part of the literature available on the biological aspects of schizophrenia, one will find several items suggesting that the adrenals form a link in the pathogenesis of schizophrenia as has been repeatedly emphasized. In schizophrenia there is a tendency to low blood pressure, reduced basal metabolic rate, and disturbances in the carbohydrate metabolism (*Hoskins, Freeman, Bowmann, Barcroft, McFarland*, and others.)

Investigating the excretion of 17-ketosteroids in the urine of normal and schizophrenic subjects, *Hoskins* found that the increase found in normal subjects in the morning was absent or only slight in

schizophrenics. Following imposed stress, such as breathing air of reduced oxygen content, exposure to hot air, and various psychomotor tests, *Hoskins* obtained increased excretion of 17-ketosteroids in the urine of normal subjects, whereas the schizophrenics remained unaffected. These findings have later been confirmed by *Hoagland*. *Gottlieb & Linder* have demonstrated that schizophrenics show a higher rise in body temperature following exposure to heat than normal subjects. This agrees with the results of *Hartmann and co-workers*, according to whom adrenalectomized rats also respond with a more marked rise in body temperature than normal rats.

Tietz & Birnbaum, in 1942, studying 29 schizophrenics during metrazol and electroshock treatment, found that the patients who benefited from the treatment exhibited a rise, whereas those patients who remained unchanged still showed small amounts of cortin in the blood and also were extremely susceptible to shock.

Cortical extracts have been tried in the treatment of schizophrenia by several workers, *inter alia* *Hoskins* and *Haynes & Carlisle*. The latter maintain that they have observed some effect in catatonic patients, but on the whole the results have been negative. Accordingly, *Hoskins* advances the theory that the adrenals do produce cortin, without, however, being capable of adapting their production to immediate requirements. This theory has received support from *Freeman*, who in collaboration with *Hoskins* has measured the rise in blood pressure in schizophrenic and normal subjects following administration of cortin. They found a rise in blood pressure in 79 per cent. of the schizophrenics and in only 18 per cent. of the normal subjects. This is a well-known phenomenon in patients suffering from some kind of hormonal insufficiency: They are more susceptible to administration of the hormone than normal subjects.

Numerous studies have been made of the carbohydrate metabolism in schizophrenia. The fasting blood sugar has been found to be somewhat varied. *Meduna*, in 1943, studying 147 schizophrenic subjects, found 83 with a blood sugar level of 75 mg. per cent. and less, whereas 64 ranged between 75 and 90 mg. per cent. In 1940 *Geller* found that 69 patients affected with so-called asthenic, autistic schizophrenia had reduced blood sugar, whereas 14 patients belonging to the hyperthymic, expansive type had slightly increased blood sugar. *Freeman*, in 1933, studied a large series of 620 subjects. A total of 76 per cent. showed values within normal limits, 9 per cent. below, and 15 per cent. above the normal. *Hoskins* arrived at a similar result. The same applies to the blood sugar tolerance: Abnormal curves, but no definite common feature, although there is perhaps some tendency to flattened

curves with prolonged, enhanced values. *Raphal*, in 1922, found prolonged, enhanced values in 37 cases of acute schizophrenia. *Tsuchiya*, in 1924, found a blood sugar curve reaching its summit in the course of 1 hour and with delayed return to normal. *Bowmann & Whitehorn* also found prolonged, enhanced values. It is stated by *Mann & Scott* in 1929 that the blood sugar tolerance curves in schizophrenia suggest delayed glycogenesis.

There do not appear to be any extensive studies on the processes of phosphorylation in schizophrenia. *Skaug & Hellem* have contributed to elucidating the problem by determining 6 of the fractions of phosphoric acid in the blood. According to them inorganic phosphorus is 19 per cent. and hexosephosphoric acid 34 per cent. lower in schizophrenic than in normal subjects. These workers compare their results with those of *Erkki Jokivartio's* studies on plasmaphosphatides in schizophrenia, which showed that a similar disturbance takes place in the lipoid metabolism, the plasmaphosphatide content in acute schizophrenia being 43 per cent. below the normal. Their conclusion is that it cannot be a question of isolated disturbance of the phosphatide metabolism, but a disturbance of the processes of phosphorylation in schizophrenia. In this connection it is not out of place to mention *Looney & Child's* finding of increased lactic acid in the blood of schizophrenics and of a higher increase in the lactic acid content of the blood upon exertion than among normal subjects. These findings have later been confirmed by *Katzenelbogen, H. Lofendahl*, and *Geller*. This latter finding is also suggestive of a disturbance of the processes of phosphorylation, as the capacity of the organism to form glucose from lactic acid depends on the amount of cortin in the blood, so that cortin deficiency is bound to inhibit or even arrest this process. Without advancing further explanations *Chase*, in 1939, demonstrated that vitamin B₁ failed to have the effect on schizophrenics that was demonstrable in normal subjects. This, too, can be attributed to cortin, as vitamin B₁ must be phosphorylated before it can exercise its action.

We now have to consider the investigations made to elucidate whether schizophrenics exhibit disturbances of the metabolism of electrolytes, especially of sodium and potassium. I have only been able to find one report, that of *Katzenelbogen & Snyder*, who studied the electrolytes, including potassium and sodium, in 29 schizophrenics. They found no divergence from normal conditions as regards sodium, whereas potassium was increased in a few cases. These results will be discussed later in the present paper. As investigations into the sodium and potassium content in the serum of schizophrenics appear to have

been reported only once. I set myself the task of studying this question in more detail.

I shall now proceed to describe my analytic technique in determining the sodium and potassium content in the blood serum and to present my normal material, which will be compared with the normal values found by earlier workers.

The serum sodium was determined according to *Kolthoff & Sandell*. Five cc. of serum were drawn into a pipette and ashed. At the outset the first part of the analysis was performed according to the method of P. M. Hald, but this had to be abandoned, as sodium was lost in the ashing process, very probably because the temperature required to burn off the carbon was so high that the sodium began to evaporate. Then I adopted another method of burning the organic material off, viz. by heating of the serum with concentrated sulphuric acid in Kjeldahl flasks and oxidation with nitrous acid. This could be accomplished without loss of sodium. After volatilization of the sulphuric acid the inorganic components which were left were dissolved in 50 cc. of water. 10 cc. of this (corresponding to 1 cc. of serum) were precipitated with 10 cc. of zinc uranyl acetate and allowed to stand for 3 hours in an ice-box. Then followed filtration through a previously weighed suction filter, and the sediment was washed and dried and then weighed. Its weight multiplied with 0.1495 gives the mg. per cent. of sodium in the serum. (Both balance and weights were sent to be adjusted, before the experiments were commenced).

Potassium was determined by the method of Peters and van Slyke. The first part of the analysis was carried out as in the sodium determination with sulphuric acid, oxidation with nitrous acid, volatilization, and dissolution in water. It must be mentioned here that after centrifugation the serum was examined for blood reaction and rejected, if a positive reaction was found. (As is well-known the potassium content of the blood is much higher in the blood corpuscles than in the plasma). 10 cc. of the solution (corresponding to 1 cc. of plasma) was evaporated to about 1 cc., precipitated with 0.3 cc. hydrogen platinum chloride and evaporated until it had the consistency of syrup. The preparation was then washed in alcohol, 80 per cent., saturated with potassium platinum chloride in order to dissolve the sodium platinum chloride formed at the same time. The fluid was poured into a small suction filter, the remaining sediment and the filter washed 5-6 times in alcohol, 80 per cent., saturated with potassium platinum chloride, until the filtrate drawn through the

- (5) 23.4 mg. %
- (6) 23.0 mg. %
- (7) 23.1 mg. %
- (8) 23.4 mg. %
- (9) 23.8 mg. %
- (10) 23.0 mg. %

Mean value = 23.3 mg. per cent.

Mean error = ± 0.277 .

The mean error of the mean value = ± 0.09 .

In other words, the error in each individual potassium analysis was about 3 per cent.

The normal material comprises the male nurses and a few female nurses from the hospital, who kindly submitted to the tests. The blood was obtained before breakfast, and I made sure that the subjects were healthy and especially that they did not exhibit any symptoms of renal disorder. (*David Ottosen* found low sodium values in a few patients with chronic nephrosis).

Double analyses were made of all the sera.

Serum sodium:

Sex	Age	Sodium mg. %	Potassium mg. %
♂	31	336.4	18.7
♂	57	337.6	20.2
♂	35	343.3	19.7
♂	28	353.0	17.5
♂	29	342.3	18.7
♂	38	335.5	21.0
♂	30	339.7	17.2
♂	21	336.2	16.8
♂	36	337.8	18.7
♂	27	332.6	18.5
♂	40	334.7	18.8
+♀	33	329.2	19.7
+♀	25	339.6	18.8
+♀	21	332.2	18.2

It will be seen that the sodium content varied from 329.2 to 353.0 mg. per cent.

Mean value = 337.9 mg. per cent.

Mean error = ± 5.82 .

Mean error of the mean value = ± 1.55 .

The potassium values varied from 16.8 to 21.0 mg. per cent.

Mean value = 18.8 mg. per cent.

suction filter was as clear as water. The sediment which then remained, partly in the filter, partly in the crucible, was dissolved in a buffer solution (4.7 Ph) and poured into a titration flask containing 3 cc. of 2 n. potassium iodide. The fluid was kept at 65° C. for 15 minutes, cooled, and titrated with 1/100 n. sodium thiosulphate in a micro-pipette until the fluid changed from red to a yellow colour. The number of ml. of sodium thiosulphate used multiplied with 39 gives the mg. per cent. potassium in the serum.

This technique was practised by analysing known solutions of sodium and potassium chloride. The error in the individual analysis was determined by serial analyses of a sodium and potassium chloride solution of known concentration.

RESULTS

Sodium chloride solution (about 8.6 g. in 1 litre).

Sodium determination:

- (1) 342.8 mg. %
- (2) 343.9 mg. %
- (3) 342.8 mg. %
- (4) 345.5 mg. %
- (5) 342.7 mg. %
- (6) 340.9 mg. %
- (7) 345.3 mg. %
- (8) 343.3 mg. %
- (9) 344.2 mg. %
- (10) 341.6 mg. %

Mean value = 343.3 mg. per cent.

The mean error was calculated according to the well-known formula

$$\delta^2 = \frac{\sum (x \div m)^2}{n \div 1} \text{ and was found to be } = \pm 1.47.$$

The mean error of the mean value was calculated according to the

$$\text{formula } \varepsilon = \frac{\delta}{\sqrt{n}} \text{ and was found to be } = \pm 0.46.$$

In other words, the error in each individual sodium analysis was about 1.3 per cent.

Potassium chloride solution (about 0.4 g. per litre).

Potassium determination:

- (1) 23.4 mg. %
- (2) 23.0 mg. %
- (3) 23.4 mg. %
- (4) 23.8 mg. %

Mean error = ± 1.15 .

Mean error of mean value = ± 0.30 .

These normal values appear to accord well with those found by earlier workers. As to sodium *Kramer* found the normal range to be between 325.9 and 350.1 mg. per cent., *Keys* 317.4 to 354.2 mg. per cent., *E. Y. King* 325 to 350 mg. per cent., and *McCance* 317.4 to 345 mg. per cent.

As to potassium *Kramer* found normal values ranging from 16 to 22 mg. per cent., *Salvesen & Linder* 19.1 to 21.8 mg. per cent., *Becker* 19 to 23 mg. per cent., and *Brems* 15.5 to 23.4 mg. per cent.

The patients are divisible into two groups, as I studied partly recent cases, i.e. psychoses of up to 2 years' standing, partly chronic cases. Each group comprises 13 patients. Before the analysis the patients were thoroughly examined, and those who exhibited signs of somatic affections, especially kidney and heart disease, were rejected. The blood was obtained under the same conditions as in the normal subjects.

Group I:

ACUTE SCHIZOPHRENIA

Case 1. (Case rec. 15337). Male, aged 24, born 2.5.23. Family history: A maternal aunt of his father's sister is suffering from "religious madness", a niece of his maternal grandfather from catatonic schizophrenia.

The eldest of 4 siblings brought up in good social circumstances. Matriculated, studied law for 3 years and passed the ordinary examinations.

Has always been in good health.

Pre-morbid personality: Has always been eccentric, seclusive, and suspicious and had difficulties in making friends.

His present illness developed gradually from the end of 1946. He grew more and more seclusive, neglected his studies, and now and then he would fly into a passion and scold his family. His condition steadily deteriorated, thought he or others were possessed by the devil, read the Bible day and night. When he entered the hospital on Oct. 9, 1947, he stated that during the last 9 months he had not been interested in his studies, but had been occupied with more serious religious problems. He described a conflict within himself between good and evil in which he was guided by voices.

On admission he was emotionally indifferent, withdrawn, and hallucinated.

During the subsequent period the patient was very resistive, negativistic, had to be fed, did not talk spontaneously and only replied by monosyllables, at times aggressive, excited, and screaming. At times he lay in a stupor, staring at the ceiling with one arm lifted. Treated with insulin without actual improvement. After this treatment the condition varied somewhat between restless and quiet periods, there was still a tendency to lie in catatonic postures. Could not be occupied. The catatonic features grew ever more marked, he would lie for hours with his arms lifted, stating that he felt better that way. On May 8, 1948, insulin was

tried again, but had to be stopped because of protracted shock. The patient remained unconscious for 48 hours. This was followed by marked improvement, but he remained indifferent, listless, and catatonic.

Laboratory tests: SR., Hb., W.r., urine blood pressure: Nothing abnormal.

Diagnosis: Catatonic schizophrenia.

The duration of the illness had been about 18 months.

10.5.1948: Serum sodium 339.7. Serum potassium 16.9 per cent.

Case 2. (Case rec. 15203). Male aged 32, born 24.8.16. Family history: Three brothers were "nervous", a brother's son admitted to this hospital as suffering from psychogenic reaction, emotional erethism. Two maternal aunts insane.

The patient had been brought up in poor circumstances and had mostly worked on farms and lately as a labourer.

Had always been healthy.

Pre-morbid personality: Had always been rather seclusive, but otherwise nothing abnormal.

The present illness set in after New Year 1947. The patient began to get restless, ran out at night, and threatened the family. Gradually he acquired several delusions, thinking that he was being persecuted, that he was going to die, that he was in connection with the celestial bodies, registered the sun, and had calculated the quadrature of the circle. He had hallucinations, hearing human and animal voices, and felt influenced by his environment.

When admitted to the hospital on June 30, 1947 the patient disclosed the same delusions. Otherwise he was friendly and polite, but often difficult to get into contact with. Treated with metrazol which resulted in transitory improvement, and in August 1947 with insulin, also resulting in improvement. However, he relapsed every time and during the last year his psychic condition has become worse. He still has marked hallucinations and is lying most of the time in a tense, threatening posture. Gives no or quite inadequate answers when addressed. Sometimes aggressive and impulsive, at times very restless, uttering screams without apparent cause. Still, he does not have to be cared for and is tidy in his habits of urination and defæcation.

No particular objective findings.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Paranoid schizophrenia.

The duration of the illness had been about 18 months.

14.6.1948: Serum sodium 331.2, serum potassium 19.7 mg. per cent.

Case 3. (Case rec. 14501). Male, aged 27, born 18.12.20. Family history: A maternal aunt has been an inmate of the St. Hans Mental Hospital for many years.

The third of 5 siblings. His home as a child good, got on normally at school, which he left at about 15, and had since then had various jobs as a labourer.

In 1945 hepatitis, otherwise negative history.

Pre-morbid personality: Fairly good-tempered.

The present illness set in about February 1946, when the patient began to make complaints of a neurasthenic nature. He did not think there was any hope for him, and gradually got more depressed and inhibited, had hallucinations in which he thought he heard the voices of his family. Entered the hospital on 26.3.46.

On admission the patient stated that he had great pain in various sites and

thought he was suffering from cancer of the larynx. He was depressed and greatly inhibited, but suddenly he would burst out laughing without apparent cause. During the subsequent period he developed several delusions, appeared to have marked hallucinations and was somewhat schizoid, gradually growing more and more silly and indifferent. He was confused, thinking that the other patients were Polish catholics. Treated with shock (electroshock) without actual improvement. The development of his psychosis had a definitely schizophrenic trend with increasing fragmentation of the mental functions, and he had bizarre and fantastic delusions. The patient spent most of the time sitting with a fatuous smile, and it was difficult to obtain a coherent answer from him. Definite hallucinations, and gradually extremely aggressive and impulsive, throwing the plates about, but could be kept tidy in his habits of urination and defæcation.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Paranoid schizophrenia.

The duration of the illness had been about 2 years.

17.3.1948: Serum sodium 338.2, serum potassium 18.9 mg. per cent.

Case 4. (Case rec. 15951). Male, aged 23, born on 7.2.25. Family history: His mother has been in hospital with paranoid psychosis and his paternal grandfather committed suicide at the age of 60.

The eldest of 3 siblings, strictly brought up, and his father often hit him. After leaving school he was trained as a waiter and had been at sea a few times.

Has on the whole been healthy. Was rejected for military service because of heart disease which, however, never had given rise to subjective discomfort. Electrocardiogram showed no definite abnormalities.

Pre-morbid personality: Always been very serious, never interested in making friends.

The present illness began in June 1947. The patient grew tired and indisposed, but still he signed on as a ship's waiter. After his return home his condition grew worse, he flew into passions and tore his clothes. On May 8, 1948, he entered the hospital.

On admission he gave his history, but was unable to concentrate on the same train of thought for any length of time. He was indifferent and denied having hallucinations.

During the subsequent period very listless, unoccupied, appeared at times to be tense, quivering. Had a few explosions during which he threw the furniture about, cried, and felt unhappy, thinking that he was going mad. He remained inaccessible, unable to concentrate. At times he exhibited bizarre, schizophrenic disturbances in association.

Treated with insulin on July 14, 1948 and alternated during the subsequent period between spells of sitting quietly, devoid of initiative, and spells of a more depressed and tense nature. No definite effect of the treatment, he remained sluggish, uninterested, and without any emotional contact. Could be occupied for a short time, but quickly lost interest.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Simple schizophrenia.

The duration of the illness had been about 1 year.

17.6.1948: Serum sodium 337.9, serum potassium 17.7 mg. per cent.

Case 5. (Case rec. 15408). Male, aged 22, born 15.5.26 Family history: Paternal grandfather committed suicide at the age of 57 and paternal grandmother suffered from spells of stolidity.

No. 2 of 6 siblings. His home as a child good. Got on well at school and afterwards helped his father on the farm.

Had always been healthy.

Pre-morbid personality: Had always been somewhat seclusive, subject to fluctuating moods.

The present illness began in July 1946. He gradually became apathetic, sitting listless in a chair, doing nothing except listening to the wireless. Entered the hospital on September 3, 1946.

On admission the patient made an impression of being very dull and listless. He could give his history, but had no insight into his condition, denied having hallucinations, ideas of being influenced, or delusions. There was distinct withdrawal, and it was at no time possible to establish emotional contact with the patient.

Treated with electroshock without improvement. He was rather preoccupied with various hypochondriacal complaints. Was on a working team, but did not do much work as he became immersed in thought at brief intervals. Did not mix with the other patients, but did not admit having hallucinations. Discharged at the end of 1946, but re-admitted on 29.11.47. Had not been well since discharge. Often sitting quietly, staring into space, grimacing, uninterested, and had had a few minor explosions. On re-admission he was just as before, apathetic, listless, and emotionally indifferent, with no insight into his condition.

On Aug. 26, 1948 insulin was started, but without effect. The treatment was interrupted, and the state has remained unchanged since then.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Simple schizophrenia.

The duration of the illness had been about 2 years.

17.6.1948: Serum sodium 342.3, serum potassium 20.7 mg. per cent.

Case 6. (Case rec. 15159). Male, aged 52, born 29.2.96. No family history.

No. 3 of 9 siblings, his home as a child good. Got on normally at school. Since then had done well as a fisherman.

On the whole healthy so far.

Pre-morbid personality: Always good-tempered, but never showed much interest in the company of others.

The present illness had an insidious onset about April 1947, when the patient began to feel persecuted by his neighbours, stating that they were spying on him and that he had heard them accuse him of criminal sexual behaviour. Several times he had burst into a violent rage, threatening those around him. Admitted on 9.6.47.

On admission the patient advanced a number of fantastic paranoid ideas, e.g. that the neighbours wanted to infect him with syphilis by sending women to him at night and that they were doing him harm by affecting him in a way which made him unable to hit the game when he was out shooting. Other people could read his thoughts and affect his heart, stop it and thus get rid of him. When admitted, he was in an angry mood, was "sure to get his revenge". No definite hallucinations.

He quickly settled down in the ward, but his paranoid ideas remained unchanged. Shock treatment was not attempted, because of electrocardiographic evidence of myocardiac degeneration. He could be made to work in the workshop, but he gradually expressed new paranoid ideas revealing that he had visual as well as auditory hallucinations. At times he was angry, hostile, and did not mix with the other patients. Seldom talked spontaneously. The condition remained unchanged.

Objective examination revealed slight cyanosis of the lips and a presystolic murmur over the apex. Otherwise nothing abnormal, no oedemas, no ascites, no increase in the liver dullness, no pulmonary congestion.

Laboratory tests: SR., W.r., Hb., urine, blood pressure: Nothing abnormal. Electrocardiogr.: Myocardiac degeneration.

Diagnosis: Paranoid schizophrenia.

The duration of the illness had been about 1 year.

28.6.1948: Serum sodium 337.0, serum potassium 22.5 mg. per cent.

Case 7. (Case rec. 15360). Male, aged 28, born 24.2.20. Family history: Three of his father's siblings feeble-minded, otherwise nothing abnormal.

His home as a child good, did badly at school. Since then engaged in farm-work, partly at home, partly elsewhere. Working capacity somewhat varied.

Healthy as a child. From 10.4 to 21.6 1947 at Rigshospitalet, Ear, Nose, and and Throat Department, suffering from acute, left-sided otitis media, mastoiditis, otitic meningitis.

Pre-morbid personality: Subject to fluctuating moods, seclusive, and eccentric.

The present illness began in June 1947. He grew increasingly apathetic and seclusive, at times suddenly burst out laughing but in the intervals was depressed and contemplating suicide.

On admission the patient made an impression of being somewhat inhibited and depressed, sticking to his plans of committing suicide. He was aware of his condition: "it feels so funny in the head". Denied having had any psychic trauma, ideas of being influenced, or delusions.

The depressed condition, however, quickly changed to the schizophrenic syndrome. He was distinctly uninterested, did not do anything, never spoke spontaneously, and seldom answered when addressed. Often he would sit about with an empty, fatuous smile, inclined to grimacing, difficult to get out of bed, negativistic, refused to work and to wear the clothes he was given, etc. Often talked aloud to himself, appeared to have hallucinations and would have explosions and attack the other patients without the slightest cause. Shock treatment was not attempted because of an increased protein content in the spinal fluid.

There were no objective signs, especially no neurological signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal. Spinal fluid: Pandy +, 7/3 cells per cmm., globulin 1, albumin 25. A repeated test showed approximately the same values.

Diagnosis: Simple schizophrenia.

The duration of the illness had been about 1 year.

28.6.1948: Serum sodium 332.8, serum potassium 22.6 mg. per cent.

Case 8. (Case rec. 14993). Male, aged 22, born 5.7.26. Family history: A maternal uncle is eccentric, otherwise nothing.

His home as a child good, did tolerably well at school, had been working on farms since age of 14.

On the whole healthy so far.

Pre-morbid personality: Fairly good-tempered.

The present illness began in the summer of 1946. The patient began to grow listless, refused to work, was easily roused, and grew more and more seclusive and silent, at times soiling himself and showing untidy habits, e.g. passing water against the wall in his bedroom.

When he stole a bicycle he was arrested and pronounced feeble-minded by the County Medical Officer and sent to an institution for mental defectives. There he was extremely listless, seclusive, and did not mix with other patients, grimacing, and inclined to stereotyped mannerisms. Once he had an emotional explosion, with some vague delusions. A diagnosis of schizophrenia was made and the patient admitted to this hospital on 24.2.47.

On admission the patient made an impression of being extremely listless, smiling in a silly way and without apparent cause, answered when addressed, stated that people could read his thoughts. Appeared to have hallucinations, was apathetic and indifferent.

During the subsequent period the patient's behaviour was very strange, characterized by peculiar mannerisms and an inclination to assume catatonic attitudes. He was not at all interested in the environment. Would often regard himself in the mirror, stating that he knew he was always changing.

At times more restless, scolding, aggressive, throwing the plates and furniture about, had to be kept in bed. In the autumn of 1947 insulin treatment, during which there was an exacerbation in his condition; he became more restless, with marked hallucinations, impulsive, and untidy in his habits of urination and defaecation.

Gradually he settled down somewhat, and could be persuaded to work, but he had to be kept going all the time, absolutely mute, laughing at times without cause, often kept up the same posture for hours.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Catatonic schizophrenia.

The duration of the illness had been about 2 years.

28.6.1948: Serum sodium 332.9, serum potassium 22.2 mg. per cent.

Case 9. (Case rec. 14552). Female, aged 31, born 9.12.16. No family history.

An illegitimate child. Childhood spent under unfavourable circumstances. After leaving school she had been employed in various factories. Married when 21 years of age and her married life had been happy. There were 2 children. Menstruation regular.

On the whole healthy up to now.

Pre-morbid personality: Good-tempered.

The present illness began in February 1946. She got various paranoid ideas, felt persecuted by her neighbours, suspected, without any cause, that her husband wanted to divorce her. Grew more and more eccentric, laughed without apparent reason, wandered about. Admitted on 25.6.46.

On admission she was disorientated as to time and place. Her mood was indifferent, she did not answer when addressed or else said, "I don't know." Expressed a few delusions, had undoubtedly hallucinations.

In the ward the patient was very listless, autistic, negativistic, and refused to be occupied. At times impulsive, and periodically aggressive, untidy in her

habits of urination and defæcation, throwing her faeces about. When it was possible to start a conversation with her she was unable to concentrate and her train of thought was incoherent. She had various, bizarre, paranoid delusions, thinking for instance that the physicians were controlling her by means of "phosphoric plates" and that they had something named "listening trail" which made them hear everything she heard and thought. She still had hallucinations and her condition remained on the whole unchanged during her stay in the hospital. In January 1948 she was referred for lobotomy.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Paranoid schizophrenia.

The duration of the illness had been about 2 years.

6.5.1948: Serum sodium 330.7, serum potassium 17.4 mg. per cent.

Case 10. (Case rec. 16212). Male, aged 31, born 17.10.17. No family history. His home as a child good, got on normally at school. Always worked on farms. Had always been healthy.

Pre-morbid personality: Well-balanced and good-tempered.

The present illness began in the autumn of 1947, when the patient began to lose interest in things and stated that he was being affected by electric currents and that strange things were going on around the house at night. Marked auditory hallucinations. Entered the hospital on 2.7.1948.

On admission the patient stated that 2 months ago he had begun to feel persecuted by various persons who threw electric currents at him and talked to him with inner voices. He had various bizarre, hypochondriacal ideas, e.g. "the nerves in the head had burst—the bowel was constricted, so that he could have no motion." When addressed he made an impression of being unable to concentrate and of being emotionally shallow. At times he was withdrawn, and had undoubtedly hallucinations.

To begin with he was extremely restless, ran around on the floor, and had no insight into his condition. Did not spontaneously express his paranoid ideas, but when the subject was brought up, they welled forth. Treated with electro-shock and later, in the autumn of 1948, with insulin, which had some effect, as he concealed his paranoid ideas better, but he remained emotionally shallow, and still had hallucinations.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Paranoid schizophrenia.

The duration of the illness had been about 1 year.

12.7.48: Serum sodium 330.0, serum potassium 18.9 mg. per cent.

Case 11. (Case rec. 16250). Female, aged 20, born 22.4.28. Family history: A brother suffering from schizophrenia.

Grew up in poor social conditions, got on normally at school. Since then worked as a housemaid. Engaged, had 1 child, born 17.4.48. Menstruation had previously been regular, but since delivery there had been menostasis.

Pre-morbid personality: Always very seclusive.

The present illness began in April 1948, when the patient began to grow more and more queer and refused to take care of her baby. Did the most silly and motiveless things. Admitted to the Psychiatric Department of Rigshospitalet

in May 1948. Complete remission after electroshock. Diagnosis: Psychosis mani-formis in puerperio. The remission was only brief, as she again got queer ideas, changed her clothes without any cause 10 times daily, at times her speech was completely incoherent, she grew more and more restless and agitated and tore her clothes. Admitted to this hospital on 29.7.1948.

On admission she was silent, dismissing, changing between tears and laughter, admitted having hallucinations. To begin with she was extremely restless, threw the plates about, emptied her bed, often lay in strange postures, burst into violent screams, laughed foolishly when addressed, did not answer, and appeared to have marked hallucinations. Treated with metrazol shock, but quickly relapsed into her usual, restless mood, being distinctly withdrawn, had several motiveless, silly outbursts of laughter, soiling herself and being untidy in her habits, one day washing her hair in the porridge. Her mood was apathetic and indifferent.

Her condition has not changed after admission. Although there have been remissions after each course of metrazol shocks, she has relapsed in the course of a few days.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal. Diagnosis: Schizophrenia.

The duration of the illness had been about 6 months.

21.9.1948: Serum sodium 338.5, serum potassium 18.9 mg. per cent.

Case 12. (Case rec. 16223). Male, aged 31, born 13.9.1917. No family history. His home as a child good. No. 1 of 2 siblings. After leaving school he was apprenticed to a joiner. In 1946 in Singapore as a recruit in the British Army.

On the whole healthy hitherto.

Pre-morbid personality: Always seclusive and very quiet.

The present illness began towards the end of 1946 with vague paranoid ideas. Admitted to a hospital in England. Diagnosis: Hebephrenia. Transferred to Denmark and admitted to this hospital on 13.7.48.

On admission he was absolutely unprogressive, inaccessible, replied with monosyllables, was disorientated for time and place, emotionally indifferent, and at times he had a senseless, fatuous smile.

Treated with electroshock resulting in brief improvement, then increasing hallucinations, appeared to be tense and quivering, numerous motiveless explosions during which he threw the furniture about, broke windows, etc. Grew more and more autistic, had to be tied in bed, refused to take food.

On Sept. 1, 1948, insulin was started, but this only made matters worse, as the patient grew increasingly resistant, negativistic, his mood silly and indifferent. Did not speak spontaneously and seldom answered when addressed.

No abnormal objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal. Diagnosis: Schizophrenia (hebephrenic type?).

The duration of the illness had been about 2 years.

21.9.1948: Serum sodium 331.0, serum potassium 19.0 mg. per cent.

Case 13. (Case rec. 16267). Male, aged 27, born 11.4.1921. No family history. No. 2 of 5 siblings. His home as a child good, did well at school. Had been employed in various factories.

Pneumonia at the age of 10, otherwise healthy.

Pre-morbid personality: Always rather seclusive, taciturn, and serious.

The present illness began in November 1947. He could not sleep at night, was unable to concentrate on reading, thought he was affected with various organic lesions, and talked at times about poison in the food. Grew more and more apathetic, at last lying in bed, dull and inactive. Admitted on 13.8.1948.

On admission the patient stated that his disease had set in in November 1947, he felt as if "everything came to a standstill in his head." He had difficulty in concentrating, and had a feeling that he had been placed outside himself. He could not think freely, as he felt that he was being watched and affected by the environment and that people could read his thoughts. Denied having hallucinations.

On admission the patient made an impression of being unprogressive and empty, but there was no autism or withdrawal. Treated from 21.8 to 8.9 1948 with electroshock and improved slightly, although he still showed depression of affect, lack of interest, stolidity, and withdrawal.

At his mother's request he was discharged on 2.10.48 as improved.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Simple schizophrenia.

The duration of the illness had been about 1 year.

27.9.1948: Serum sodium 332.2, serum potassium 21.3 mg. per cent.

TABLE 1.
Results of the analyses in acute schizophrenia:

Diagnosis	Sex	Age	Sodium mg. %	Potassium mg. %
(1) Catatonic schizophrenia	♂	24	339.7	16.9
(2) Paranoid schizophrenia	♂	32	331.2	19.7
(3) Paranoid schizophrenia	♂	27	338.2	18.9
(4) Simple schizophrenia	♂	23	337.9	17.7
(5) Simple schizophrenia	♂	22	342.3	20.7
(6) Paranoid schizophrenia	♂	52	337.0	22.5
(7) Simple schizophrenia	♂	28	332.8	22.6
(8) Catatonic schizophrenia	♂	22	332.9	22.2
(9) Paranoid schizophrenia	♀	31	330.7	17.4
(10) Paranoid schizophrenia	♂	31	330.0	18.9
(11) Schizophrenia	♀	20	338.5	18.9
(12) Schizophrenia (heb. ?)	♂	31	331.0	19.0
(13) Simple schizophrenia	♂	27	332.2	21.3

Serum sodium: Values ranging from 330.0 to 342.3 mg. %

Mean value: 335.0 mg. %

Mean error = ± 4.16 .

Mean error of mean value = ± 1.2 .

Serum potassium: Values ranging from 16.9 to 22.6 mg. %

Mean value: 19.7 mg. %

Mean error = ± 1.97 .

Mean error of mean value = ± 0.55 .

Group II:

CHRONIC SCHIZOPHRENIA

Case 1. (Case rec. 15148). Male, aged 29, born 5.2.1919. Case rec. fails to give any details about family history.

No details about childhood or school. After leaving school trained as a waiter, 1938-39 in America.

On the whole healthy hitherto. Uncomplicated gonorrhoea in 1937.

No information about pre-morbid personality.

The present illness began in 1939 during a stay in America. One day he addressed a policeman and asked him to remove a man who was walking beside him. As there was no man beside him and the patient's behaviour was extremely strange, he was sent to a mental hospital where he stayed until 1947, when he was transferred to Denmark and admitted to this hospital on 3.6.1947.

On admission he was completely indifferent, unable to concentrate, spoke incoherently, had no insight into his condition, and denied having hallucinations or ideas of being influenced. No withdrawal or autism.

In the ward the patient was very restless, wandering aimlessly about, often in silly high spirits, whistling and laughing without any cause whatever. Was started in the workshop, but without success, because of his restlessness. Treated in 1947 with insulin without effect. Seldom talked spontaneously, but answered when addressed, his speech being incoherent, disconnected and gibbering, his mood indifferent and apathetic.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Hebephrenia.

The duration of the illness had been about 9 years.

6.7.1948: Serum sodium 339.9, serum potassium: 17.2 mg. per cent.

Case 2. (Case rec. 14097). Female, aged 23, born 16.1.1925. No family history. An illegitimate child, grew up with her mother. Left school at 14 and received no further training.

On the whole healthy hitherto, menstruation regular.

Pre-morbid personality: Well-balanced and good-tempered.

The present illness began in 1943, when the patient began to lose interest in things, refused to work, secluded herself, heard voices, expressed vague paranoid ideas and a number of hypochondriacal complaints. On 28.7.1945 she entered this hospital.

On admission she was very shallow emotionally, unable to concentrate much, laughed in a silly way when spoken to, disorientated for time and place.

In the ward she was usually unoccupied, never spoke spontaneously, appeared to have hallucinations, refused to take food periodically, contrary, negativistic, untidy in her habits of urination and defæcation, soiled herself with fæces, took off all her clothes, took to screaming a few times, stopping her ears with cotton wool and cellulose wadding. Treated with metrazol without improvement.

Gradually getting more and more queer, having bizarre ideas, more and more apathetic, had to be cared for, getting increasingly catatonic, sitting for hours in peculiar, rigid postures.

Periodical, prolonged catatonic spells of excitement during which she shouted

and screamed, threw the plates about, attacked those around her, and had marked hallucinations.

During the last few years the condition has remained completely unchanged. At times shock treatment has been tried, but without effect.

No abnormal objective signs demonstrable.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Catatonic schizophrenia.

The duration of the illness had been about 5 years:

12.7.1948: Serum sodium 333.7, serum potassium 19.1 mg. per cent.

Case 3. (Case rec. 13731). Female, aged 35, born 24.9.1913. Family history: Her father once treated for a psychogenic depression, otherwise negative.

The youngest of 3 siblings. Her home as a child good, got on normally at school. Later trained as a dancer and actress. Has performed a good deal abroad, *inter alia* in Paris, London, and Berlin.

Poliomyelitis with transitory paralysis at the age of 16, otherwise healthy.

Pre-morbid personality: Had always been childish and subject to fluctuating moods.

The present illness began in Paris in 1939 with paranoid ideas. The patient felt persecuted and left France, but in Denmark she could not feel at ease either, was tired and indisposed, grew ever more seclusive. Admitted to various psychiatric departments from 1939 to 1944. Her condition deteriorated, getting more schizophrenic. Apathetic, refused to be occupied, was impulsive, aggressive, and had hallucinations. Would often burst into senseless laughter. In 1944 the patient entered this hospital.

Her condition was marked by lack of initiative, poverty of ideas, stereotypy, and inner restlessness, as a rule she was rather autistic, with periods of withdrawal, seclusive tendencies, had to be urged to do every single thing, seldom talked spontaneously. Occasionally she could be made to do some needlework. At times she had violent attacks of excitement, shouting and screaming, gesticulating wildly, and stamping the floor, giving the explanation that she felt as if her eyes were being pulled out or as if she were being connected with a machine.

Treated periodically with metrazol and electroshock without effect any length of time.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Schizophrenia (type uncertain).

The duration of the illness had been about 9 years.

12.7.1948: Serum sodium 332.9, serum potassium 18.3 mg. per cent.

Case 4. (Case rec. 7563). Male, aged 48, born 8.2.1900. Family history: A maternal as well as a paternal uncle died in a mental hospital. Diagnoses not known.

No details about his home or schooling.

After leaving school he was apprenticed to a gardener. Now a skilled gardener. On the whole he had been healthy except for convulsions during infancy.

Pre-morbid personality: Well-balanced and good-tempered.

The present illness began about 1915 when the patient began to be taciturn, seclusive, avoiding those of his own age, could at times fly into violent tempers. As time went by he had to give up his job as a gardener and lived with his family.

His disease progressed, he grew increasingly apathetic, refused to be washed or change his underclothes, had numerous, sudden explosions without apparent reason, hitting his family or spoiling the furniture. On 30.9.1921 the patient was admitted to this hospital.

On admission he was extremely listless, and dull, seldom answered when addressed, distinctly withdrawn, fairly orientated in his own history, but disorientated for time and place, denied having hallucinations, had no insight into his condition.

In the ward the patient at first seemed to be very dull, of an indifferent, blank mood, autistic, with occasional sudden explosions, attacks of excitement, with shouting and screaming. Could not be occupied. During the subsequent years the condition remained completely unchanged. He would sit stooping on a bench doing nothing, and only swaying to and fro in a stereotyped manner or stand for hours in the same position, leaning against the wall. Gradually he got more and more untidy in his habits of urination and defæcation, he never spoke spontaneously and seldom answered when addressed. No definite hallucinations.

During recent years there have been no explosions. The patient appears to be utterly deteriorated and demented.

Never treated with shock until 1948 when electroshock was tried without effect.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Catatonic schizophrenia.

The duration of the illness had been about 33 years.

22.7.1948: Serum sodium 327.6, serum potassium 17.6 mg. per cent.

Case 5. (Case rec. 12759). Male, aged 31, born 5.8.1917. Family history: A maternal aunt had suffered from spells of depression, otherwise negative.

His home as a child good, got on normally at school. Since the age of 14 he had been working on farms.

On the whole he had been healthy hitherto.

Pre-morbid personality: Fairly good-tempered.

The present illness set in suddenly about February 1938, when the patient was shaken with a violent crying fit, his entire body quivering. The following night he ran into the neighbour's field and had to be brought back by force. Was unable to explain his conduct. Admitted on 24.3.1938.

On admission he appeared to be anxious and distressed. Admitted that he had had hallucinations for a long time, had a feeling that "someone was taking his thoughts." Stated that he had been ill for a couple of years, but could not explain his illness, "had had strange thoughts."

In the ward he was somewhat restless, walking up and down, undoubtedly having hallucinations, showed strange mannerisms, often lying in peculiar attitudes, staring into space. Only seldom talked spontaneously and gave a short answer when addressed. Metrazol shock without improvement.

In a few periods he was explosive and excited, impulsive, but on the whole he gradually became more and more apathetic, being autistic and having to be urged to do every little thing, often burst into senseless laughter. Two courses of insulin treatment (1939 and 1943) without improvement. Since 1943 the condition has been fluctuating, in periods impulsive, aggressive, hitting the staff and the other patients, in other periods it has been as if the patient has become completely

unprogressive, refusing to do anything, standing all day long in the same place in catatonic, rigid attitudes, inaccessible, resistant and negativistic, soiling himself, and untidy in his habits of urination and defæcation.

No abnormal objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Catatonic schizophrenia.

The duration of the illness had been about 10 years.

22.7.1948: Serum sodium 332.7, serum potassium 17.4 mg. per cent.

Case 6. (Case rec. 11917). Male, aged 35, born 27.5.1913. Family history: His mother had been melancholy during the menopause, otherwise negative.

Small means in his home as a child, went to school up to the age of 14, since then a stoker.

On the whole healthy hitherto.

Pre-morbid personality: Always well-balanced and good-tempered.

The present illness began in 1935, when the patient began to be ever more quick-tempered, rough, and dismissing. Lost interest in his work and would at times lie in bed, dull and apathetic. Admitted on 30.4.1940.

Seemed somewhat dismissing and angry, lay in bed doing nothing. Not definite hallucinations, no delusions. As the patient refused to take food, he had to be fed with a tube. Gradually he quieted down, but still refused to be occupied, showed a tendency to assume certain postures, spent much time in front of the mirror. Metrazol treatment with some improvement.

Discharged on trial after 1 year in the hospital, but returned within a month, as he had threatened his mother. On re-admission he advanced some high-flown ideas about some discoveries he was about to make, but quickly forgot them. Could not be persuaded to do anything, would stand most of the day leaning against the wall, not talking spontaneously. At the end of 1941 insulin treatment was tried, but without success. The treatment was repeated in 1942, with the same negative result. The patient grew increasingly apathetic, showing marked catatonic behaviour, lying for hours on his bed with his legs dangling over its edge. Had to be helped dressing, was untidy in his habits of urination and defæcation and had periodically to be fed.

A few explosions, but on the whole the condition is marked by catatonic attitudes, pronounced autism, and lacking emotional contact.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Catatonic schizophrenia.

The duration of the illness had been about 13 years.

22.7.1948: Serum sodium 330.7, serum potassium 18.5 mg. per cent.

Case 7. (Case rec. 14057). Male, aged 56, born 12.11.1892. Family history: A maternal uncle given to drink, otherwise negative.

No details about his home as a child. Got on normally at school. Had been working on farms since the age of 14.

On the whole healthy hitherto.

No details about pre-morbid personality.

The present illness set in about 1917, when the patient began to be dispersed, taciturn, and seclusive. During the period immediately before admission he grew more explosive, hitting those around him on the slightest provocation. Admitted on 6.2.1919.

On admission he was in a friendly mood, admitted that he had been hearing voices for a long time and had been unable to collect his thoughts. Denied having ideas of persecution.

In the ward his mood fluctuated, at times he was manageable and quiet, at other times angry, aggressive, refusing to obey the regulations. He had hallucinations, often laughed senselessly, but appeared to realize his condition to some extent. Discharged in 1920, but re-admitted 2 months later because of emotional explosion. After that he remained in the hospital for 3 years during which period his condition remained as described above. Then he was discharged and did not return until 1934. In the meantime his disease had been progressing. The patient had grown more and more deranged, having various paranoid ideas. The neighbour's evil thoughts were being thrown at him in the form of diseases, he was in possession of supernatural strength, was able to fly through the air, was at times transformed halfway into a horse. He kept elaborate records of his numerous strange adventures and wrote to the Pope about them. Had marked visual as well as auditory hallucinations. As he hit a member of his family in 1934, he was hospitalized again. Made an impression of being distinctly paranoid, advancing several bizarre ideas and telling about strange visions. Admitted that he was hearing voices all the time.

In the ward he was quiet, often occupied with writing which revealed numerous delusions, *inter alia* that his family was of royal birth and that he himself was an almighty spirit on earth. Divided the universe into various worlds, of which there were supposed to be four, he himself living in the fourth.

The condition has remained quite unchanged. He can be made to work at painting in the workshop. His mood is neutral, there are no explosions, but visual and auditory hallucinations. He is still occupied with writing elaborate reports on his paranoid ideas.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Paranoid schizophrenia.

The duration of the illness had been about 31 years.

21.9.1948: Serum sodium 328.6, serum potassium 19.2 mg. per cent.

Case 8. (Case rec. 15510). Male, aged 39, born 1.7.1909. No details about family history.

His home as a child good, left school at 14, intelligence below normal. Has since then been working on farms.

At the age of 15 hemicastration following trauma, otherwise nothing.

Pre-morbid personality: Generally good-tempered.

The present illness had been developing gradually since 1943. The patient grew ever more suspicious and seclusive, thinking that people were talking evil of him, and that he was receiving warnings over the wireless that he would be killed. One evening he had seen a fireball flying past him and this he also interpreted as a warning of violent death. As time went by he did not dare to stay at home, but he did not either feel safe among his friends, as he thought they looked as if they were in the plot. Admitted on 7.12.1946.

On admission his mood was neutral, he was orientated for time and place, advanced his numerous paranoid ideas without being in any great excitement about them. Admitted hearing voices. Had no insight into his condition.

In the ward he was calm and quiet. When addressed he advanced his ideas of persecution at once. Went on demanding to be discharged to talk to the police: "the truth must out." Wanted to go to England to have an injection of "truth serum". Treated with metrazol shock without effect.

In the course of the following year his paranoid ideas grew ever more bizarre. He was a second Christ, destined to carry the burdens of humanity. At times he was threatening and tense, but otherwise on the whole more apathetic and devoid of feeling. In periods he could be made to work. Insulin treatment without any effect in May 1948.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Paranoid schizophrenia.

The duration of the illness had been about 5 years.

27.9.1948: Serum sodium 331.9, serum potassium 17.8 mg. per cent.

Case 9. (Case rec. 12244). Male, aged 29 born 2.7.1919. Family history: A maternal aunt committed suicide, otherwise no details.

His home as a child good. Matriculated with fairly good marks. Attended an officer's school, but left and began studying law.

On the whole healthy hitherto.

No details about pre-morbid personality.

The present illness began in the autumn of 1940 with ideas of persecution, as he thought that his tutor was doing everything to annoy him, that everything had a double meaning. Gradually these ideas were also extended to the professors during the lectures. He also thought that the wireless was sending out reports about him. He grew ever more misinterpreting and was admitted on 10.3.1941.

On admission he was clear and orientated for time and place, distinctly paranoid with a suspicious "I know better" look. Talked freely about his history, had no insight into his condition, admitted hearing voices.

During the subsequent period he was calm and quiet, all the time producing new paranoid ideas of a bizarre nature directed against the physicians. They were hypnotizing him and giving him strange injections. Said that it was as if the thoughts were moving in the front part of his head.

Treated with insulin, at the beginning with some improvement, seemed to be able to correct some of his ideas, but quickly relapsed and again expressed his ever changing bizarre, paranoid ideas. His condition remained unchanged for a few years, but then the patient grew ever more inactive and listless, preferred to remain in bed, and could only be occupied with difficulty. Did not talk spontaneously, seldom answered when addressed. In periods aggressive, breaking windows and had to be placed in a girdle. During the last year the condition has, however, become more that of complete deterioration, the patient being autistic, unoccupied, soiling himself, and untidy in his habits of urination and defæcation.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Paranoid schizophrenia.

The duration of the illness had been about 8 years.

19.10.1948: Serum sodium 332.6, serum potassium 19.9 mg. per cent.

Case 10. (Case rec. 12804). Male, aged 35, born 25.11.1912. Family history: The patient's paternal great-grandmother had been insane, a paternal aunt "queer".

Always been healthy hitherto.

Pre-morbid personality: Heavy, reticent, and seclusive.

The present illness began in 1934 when the patient began to be more seclusive than ever, wandering about, and acting in a threatening way, wanted to kill various persons, had hallucinations, particularly auditory. Admitted on 19.8.1935 after having assaulted his parents.

On admission his mood was indifferent. He was not quite orientated for time, appeared to be remote, had no insight into his condition, denied having hallucinations. Advanced some bizarre delusions, saying for instance that his physician had given him 1500 injections into the head, making him nearly unconscious, that he had been here several times while unconscious and that it had been in the papers.

To begin with he could occupied with joinery, but lost interest. Remained disorientated for time and place, did not know the names of the nurses and physicians. Grew increasingly apathetic, inclined to assume strange postures, at times untidy in his habits of defæcation and urination. Followed a downhill course, and gradually it was impossible to occupy him, he would sit quite apathetic and stooping, showing peculiar mannerisms. Answered seldom when addressed or uttered a stereotyped "I don't know." At times he would get into a state of violent catatonic excitement, screaming and yelling, assaulting those around him. Had to be tied in bed.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Catatonic schizophrenia.

The duration of the illness had been about 14 years.

19.10.1948: Serum sodium 329.2, serum potassium 21.5 mg. per cent.

Case 11. (Case rec. 13863). Male, aged 35, born 19.3.1913. No family history.

His home as a child good. Got on normally at school. Later he had various jobs on farms and did well. Rejected for military service because of heart disease.

Had on the whole been healthy and had not had any discomfort on account of his heart disease.

Pre-morbid personality: Rather heavy and seclusive.

The present illness began in May 1940 with fatigue and indisposition. As he got more and more apathetic he was hospitalized on 30.10.1940.

On admission the patient was listless and apathetic, and he had no insight into his condition. Did not appear to have hallucinations and did not disclose any delusions.

During the subsequent period he got even more apathetic, lying in peculiar postures, almost stuporous with his head lifted from the pillow. Gradually he became more free, answering with monosyllables, but did not talk spontaneously. Had to be helped with his dressing and admitted having auditory hallucinations.

Treated with insulin without effect. Treatment repeated in 1942 resulting in some improvement as the patient became more easy in his manners and read the papers. The improvement persisted, and he was given thyroïdin, 200 units 3 times daily with further improvement, and he was discharged in 1943, but remained under control.

At the end of 1944 he was, however, re-admitted as he had relapsed. He was now as previously listless, catatonic, untidy in his habits of urination and defæcation, lying in periods in a state of stupor, could only seldom be persuaded to work in the garden and then had to be urged on all the time.

No particular objective signs, especially no cardiac disorder demonstrable.
 Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.
 Electrocardiogram: Nothing abnormal.
 Diagnosis: Catatonic schizophrenia.
 The duration of the illness had been about 8 years.
 19.10.1948: Serum sodium 327.9, serum potassium 19.3 mg. per cent.

Case 12. (Case rec. 11993). Male, aged 58, born 21.11.1890. No details about the family history.

No details about his home as a child and schooling. After leaving school trained as a mechanic and stoker.

Uncomplicated gonorrhoea in 1914, otherwise nothing.

No details about pre-morbid personality.

The present illness began in 1919 with ideas of persecution. In 1924 he was admitted to the Mental Hospital near Århus, where his condition was distinctly paranoid. He felt persecuted by the police and the ministers, talked about "brain connections" destroying his brain and forcing him to see "faces in his internal consciousness". He had a feeling that others could see and take his thoughts. Advanced delusions of grandeur, said that he was the deputy of Christ, intended to create laws for people, etc. On 2.7.1940 the patient was transferred to this hospital.

On admission he was clear and orientated for time and place. His mood was indifferent. He at once advanced a vast number of delusions as described above. In addition, he said that he had not had a motion for 40 days, as somebody had sewn his bowel up. Admitted hearing voices which talked to him at short and long distance through a "wireless brain connection".

His condition remained unchanged. Only he is now more schizoid and his paranoid ideas hardly as fanciful as before. He can be made to weave and is easy to get on with.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood pressure: Nothing abnormal.

Diagnosis: Paranoid schizophrenia.

The duration of the illness had been about 29 years.

26.10.1948: Serum sodium 336.1, serum potassium 18.9 mg. per cent.

Case 13. (Case rec. 14873). Male, aged 34, born 8.2.1914. No family history. His home as a child good. Got on normally at school, after leaving school trained as a joiner.

On the whole he had been healthy hitherto.

Described as a rather eccentric, wilful, and self-opinionated person.

The present illness began in 1939, when the patient was admitted to Rigs-hospitalet, Psychiatric Department, as he was found in the street without his trousers. Discharged a few months later, but was not well. Grew ever more taciturn and seclusive, dispersed, only answering after a long latent period, doing writing and calculations which nobody could make head or tail of. Entered this hospital on 23.2.1940.

On admission the patient was orientated for time and place, answered when addressed and all the time returned to "when the police took me in 1938". Could be diverted for a time, but still returned to the same subject. His mood was neutral and he did not appear to have hallucinations.

During the subsequent period he was subject to fluctuating moods, being at times angry, scolding, talking about the misdoing of the police towards him, demanding to be discharged at once. Gradually he advanced several bizarre religious delusions, stating that he was governed by the stars, that he had received various omens from God meaning that he was designed to save the world for which end he had devised a perpetual motion machine.

Insulin treatment without effect. Then followed a period during which he was more excited, scolding having hallucinations, advancing his queer delusions, working at his perpetual motion machine, accusing the staff of having used violence against him. The police still haunted his consciousness, he had been used as an "experimental animal" by the police. Wrote long letters to his family describing his various religious delusions. Was at times extremely untidy, soiling himself with his faeces, spitting, and seldom doing any work.

During the following years he grew even more dull and uninterested, did not answer when addressed, did not talk spontaneously, and did not talk about his delusions. Impossible to persuade to work. Treated with metrazol without effect.

In the course of the last year or so there appears, however, to have been a slight improvement, as he can be persuaded to work, has become tidy in his habits of urination and defæcation, only occasionally advances his delusions, and there are only a few minor explosions. Otherwise his mood is on the whole quite indifferent and apathetic.

No particular objective signs.

Laboratory tests: SR., Hb., W.r., urine, blood, pressure: Nothing abnormal.

Diagnosis: Paranoid schizophrenia.

The duration of the illness had been about 9 years.

26.10.1948: Serum sodium 336.1, serum potassium 17.4 mg. per cent.

TABLE 2.

Results of the analyses in chronic schizophrenia:

Diagnosis	Sex	Age	Sodium mg. %	Potassium mg. %
(1) Hebephrenia	♂	29	339.9	17.2
(2) Catatonic schizophrenia	♀	23	333.7	19.1
(3) Schizophrenia	♀	35	332.9	18.3
(4) Catatonic schizophrenia	♂	48	327.6	17.6
(5) Catatonic schizophrenia	♂	31	332.7	17.4
(6) Catatonic schizophrenia	♂	35	330.7	18.5
(7) Paranoid schizophrenia	♂	56	328.6	19.2
(8) Paranoid schizophrenia	♂	39	331.9	17.8
(9) Paranoid schizophrenia	♂	29	332.6	19.9
(10) Catatonic schizophrenia	♂	35	329.2	21.5
(11) Catatonic schizophrenia	♂	35	327.9	19.3
(12) Paranoid schizophrenia	♂	58	336.1	18.9
(13) Paranoid schizophrenia	♂	34	336.1	17.4

Serum sodium: Values ranging from 327.6 to 339.9 mg. per cent.

Mean value: 332.3 mg. per cent

Mean error = ± 3.61 .

Mean error of mean value: = ± 1.00 .

Serum potassium: Values ranging from 17.2 to 21.5 mg. per cent.
 Mean value: 18.6 mg. per cent.
 Mean error = ± 1.22 .
 Mean error of mean value = ± 0.34 .

DISCUSSION

It will be seen from the results of the sodium analyses in Group I (acute schizophrenia) that the values range from 330.0 to 342.3 mg. per cent. In other words, all the values are within normal limits, i.e. the mean value found in the normal material $\pm 3 \times$ the mean error. The mean value, 335.0 mg. per cent., is slightly lower than the mean value in the normal material, but this difference is counterbalanced by the maximum error which may attach to the mean value. This means that the serum sodium in the acute cases was rather low as a mean value, but not definitely abnormal.

In Group II (chronic schizophrenia) the sodium values ranged from 327.6 to 339.9 mg. per cent., i.e. within normal limits. The mean value of 332.3 mg. per cent., on the other hand, appears to be lower than the mean value in the normal material. Even when regard is paid to the maximum error on both values there is a difference which makes the mean value representing chronic schizophrenia about 1 per cent. lower than the mean value in the normal material.

In other words, the sodium values among the chronic patients are all within normal limits, but the mean value is 1-2 per cent. below the mean value in the normal material.

The potassium values in the acute cases ranged from 16.9 to 22.6 mg. per cent., mean value 19.7 mg. per cent. In this case also the individual results do not differ with certainty from the normal values. The mean value is slightly higher than the mean value in the normal material (19.7 as compared with 18.9 mg.). Still, the two figures are tangent to each other, when regard is paid to the maximum error on both values with opposite signs.

The potassium values in the chronic cases ranged from 17.2 to 21.5 mg. per cent., mean value 18.6 mg. per cent. In other words, the individual values as well as the mean value accord with the results in the normal material.

I shall now briefly compare my results with *Katzenelbogen's*. Among a series of 29 schizophrenics he did not find anything abnormal as far as the sodium content of the blood was concerned. Comparing the individual results with a normal material, he found that all the values were within normal limits. No calculation was made of the

mean values. Such a calculation shows that they do not either differ with certainty (schizophrenic subjects: 312.7 mg. per cent. $\pm$ 2.3, normal subjects: 315.7 mg. per cent. $\pm$ 3.0). In *Katzenelbogen's* material the mean error on the mean values is slightly higher than in mine, as his individual values varied within wider limits than mine.

Katzenelbogen found that the potassium values ranged from 16.0 to 26.5 mg. per cent. among the patients, whereas the controls exhibited values from 15.6 to 23.8 mg. per cent. According to *Katzenelbogen* 5 patients showed slightly enhanced potassium values, or 25 to 26.5 mg. per cent. I do not quite agree with him that these values are enhanced, as a calculation of the mean error on both sets of values shows that it is $\pm$ 3.2 for the patients and $\pm$ 2.5 for the normal subjects. In order to be enhanced the individual value must be higher than the mean value in the normal material, which in this case was 20.7 mg. per cent. $+ 3 \times$ the mean error, which means that a value must exceed 27.5 mg. per cent. to be called definitely enhanced. The mean values did not either differ essentially (schizophrenics 21.1 mg. per cent. $\pm$ 0.6, normal subjects: 20.7 mg. per cent. $\pm$ 0.7).

It will be seen from my investigations that in schizophrenia, particularly of long standing, there is a tendency to a low content of sodium in the blood. The potassium content, on the other hand, does not appear to be definitely altered. The values in the acute cases are high, but not definitely pathological.

It is probably not justifiable to draw any definite conclusions from the material, as it is not particularly large, but the low sodium values can only be taken to support the theory that the adrenals constitute a link in the pathology of schizophrenia. The variations are not so marked that the individual values are low enough to be pathological. This was not either to be expected, as it would rapidly lead to dehydration with prerenal uræmia and peripheral circulatory collapse, i.e. symptoms identical with those of untreated Addison's disease. The same appears to apply to the serum sodium in schizophrenia as to hæmoglobin, blood pressure, and metabolic rate, the individual values cannot be said to be definitely reduced, but if a number of values are compared with a control material, the mean value is lower in the schizophrenic group.

Adrenal function appears to be inhibited in schizophrenia. The glands are functioning on a basal level and do not seem capable of adapting their output to immediate requirements.

It goes without saying that schizophrenia is not caused by the mere insufficiency of the adrenal cortex. The biological picture of schizophrenia is more complicated. Various features cannot at all be

explained by cortical insufficiency, such as the diminished susceptibility to insulin; in cortical insufficiency one would expect the reverse. Moreover, a definite cure has never resulted from treatment with extracts from the adrenal cortex. However, numerous earlier investigations, receiving further support from my results, appear to suggest that adrenal dysfunction, leading to inhibition of all processes of phosphorylation in the body, is of significance to the further development of the psychosis. This is not at all surprising when it is borne in mind that the metabolism of the brain which is effected at a respiratory quotient of 1, i.e. a pure carbohydrate metabolism, cannot function in the normal way as the breakdown of glucose depends on constant phosphorylation and dephosphorylation of the cell ferments di- and triphosphopyridinenucleotide.

It has been said that schizophrenia is a pluriglandular dysfunction.

This view receives support *inter alia* from the almost ever present fibroses indicating degeneration of the pituitary, thyroid, testes, ovaries, and adrenals. Still, hormone therapy has never led to definite results, apart from thyroidin treatment which some workers have used with success. In this connection it is interesting to note that *Grollman* in his "Essentials of Endocrinology" states that administration of thyroidin induces enlargement of the adrenal glands and increased function of the cortex. In his opinion this effect is a secondary consequence of the enhanced metabolism.

It is impossible to state with certainty whether the fibroses encountered in the testes and ovaries are due to adrenal hypofunction; they may be a result of dysfunction, as *inter alia Carr & Connor* have demonstrated fibroses in the testes and ovaries of adrenalectomized rats.

The starting mechanism of schizophrenia—the precipitating factor—remains a problem. The adrenal glands do not appear to be of any significance in this respect. On the other hand, the glands seem to exert a secondary influence on the symptomatology and particularly on the biology of schizophrenia because of the reduced function.

SUMMARY

First the writer gives an account of the hormonal function of the adrenal glands, especially the mode of action of the cortical hormone. Then follows a review of part of the literature available on the biological aspects of schizophrenia, particularly that dealing with adrenal dysfunction. The technique used in determining serum sodium and serum potassium is described and an account is given of the accuracy

of the analysis and the calculations in determining the mean error on each individual analysis and the mean error on the mean value.

The normal material is presented. The results of the analyses show that serum sodium ranges from 329.2 to 353.0 mg. per cent., mean value 337.9 mg. per cent. ± 1.55 . Serum potassium ranges from 16.8 to 21.0 mg. per cent., mean value 18.8 mg. per cent. ± 0.30 . All the results accord well with the findings of earlier workers.

After reporting the case histories the writer proceeds to give the results of the analyses among the schizophrenic patients who were divided into 2 groups, Group I including recent cases i.e. psychoses of up to 2 years' standing, and Group II, psychoses of longer duration. In Group I the serum sodium ranges from 330.0 to 342.3 mg. per cent., mean value 335.0 mg. per cent. ± 1.2 , whereas serum potassium ranges from 16.9 to 22.6 mg. per cent., mean value 19.7 mg. per cent. ± 0.55 . In Group II serum sodium ranges from 327.6 to 339.9 mg. per cent., mean value 332.3 mg. per cent. ± 1.00 , whereas serum potassium ranges from 17.2 to 21.5 mg. per cent., mean value 18.6 ± 0.34 .

Discussing the results the writer arrives at the conclusion that as far as serum sodium is concerned all the individual values are within normal limits, whereas the mean value representing the acute and particularly the chronic cases is lower than the mean value found in normal subjects. Serum potassium does not appear to show any definite abnormality. The mean value representing the acute cases is rather high compared with the mean value in the normal material, but not high enough to be pathological.

The results are interpreted as a further support of the theory that the adrenal glands are a link in the pathogenesis of schizophrenia without, however, being an active factor in starting the process.

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ACUTE SHOULDER NEURITIS

A syndrome characterized by pain, paralysis, and
muscular atrophy

Description of 8 cases

By

OLLE HÖÖK

In the course of the years 1941-1945 an unusual shoulder-girdle syndrome, afterwards described by different authors under varying designations, was observed among the British and American military forces. Thus, Burnard and Fox (1942) reported 9 cases of "Multiple neuritis of the shoulder girdle". Spillane (1943) described 46 cases of "Localised neuritis of the shoulder girdle". Turner (1944) reported 36 cases of "Acute brachial radiculitis"; Weinstein (1947) 18 cases of "Localized nontraumatic neuropathy in military personnel"; Parsonage and Turner (1948) 136 cases of "Neuralgic amyotrophy—the shoulder-girdle syndrome", the last-mentioned work also including the 36 cases previously described by Turner.

The syndrome is characterized mainly by the following features:—

In almost all cases the initial symptom is a usually very sudden onset of intense pain in the affected shoulder, as a rule most intense along the upper edge of m. trapezius as well as over mm. spinati and m. deltoideus. Occasionally there is also pain along the vertebral edge of the scapula or at the axilla. Rather frequently the ache radiates down the arm and sometimes up towards the nape. This acute painful stage usually lasts 3-14 days, whereupon the ache quickly subsides, though in exceptional cases chronic pain persists.

Muscular weakness usually supervenes about 4 or 5 days after the onset, occasionally even on the 1st or 2nd day, and rarely after an interval of a few weeks. The paralyses, which as a rule are most marked at an initial stage, are of a peripheral type. Fascicular twitches have never been observed.

Muscular atrophy as a rule develops very rapidly, is usually considerable, and in such cases persistent; in less marked cases, however, a gradual improvement may be observed. Though the disease tends to affect one side only, cases of bilateral, but asymmetric affection have been reported. The muscles chiefly affected are *mm. spinati*, *deltoideus*, and *serratus magnus*, but also other muscles of the shoulder and arm may be involved.

The disturbances of sensibility are as a rule slight as compared with the paralysis, being usually confined to the outer part of the upper arm, corresponding to the innervation area of the axillary nerve.

Variations in this general syndrome have been reported. In 19 of Spillane's cases and 43 of those described by Parsonage and Turner the only muscles affected were those innervated by a single peripheral nerve, usually *n. thoracalis longus*, with resulting palsy of *m. serratus anterior*. In a few of the last-mentioned cases, besides weakness in various shoulder muscles, paralysis of *m. flexor longus pollicis* or the head of *m. flexor profundus digitorum* occurred, with resulting inability to flex the thumb or the index finger. In the casuistics of the two last-mentioned authors cases occurred in which the resulting lesions could not be explained merely by injury to one or to multiple nerves, but in which spinal roots and, in certain cases, the spinal cord had presumably been affected.

Surprisingly little has previously been published about this syndrome. Kinnier Wilson (1940) describes cases of shoulder-muscle paresis in which muscles innervated by a single nerve had been affected. Most frequently there was neuritis of *n. thoracalis longus* with consequent isolated *serratus magnus* palsy, more rarely isolated neurites of the circumflex or suprascapular nerves. These neurites had usually been preceded by infectious diseases, such as typhoid fever, pneumonia, etc. Russel Brain (1942) under the title of "Spinal neuritis" describes an interstitial neuritis which is stated to affect the fifth and sixth cervical nerves as they pass through their intervertebral foramina. This condition seems to be similar to or possibly identical with the syndrome described in this paper. Richardson (1942) drew attention to the steadily increasing cases of *serratus magnus* palsies in British neurological material. His nine cases, besides palsies of *m. serratus magnus*, also include two cases of paralysis of other shoulder muscles. In one of these two cases the patient had just received an injection of serum, whence the case must be regarded as a serum neuritis; the other case is presumably identical with the above-described shoulder-girdle syndrome.

AUTHOR'S OWN MATERIAL

In the course of the period 1945-1949 8 cases of shoulder-girdle syndrome have been observed at the Serafimerlasarett. Three of them were treated at the nerve clinic; one at the outpatient department for nervous diseases; two cases were kindly placed at my disposal by Professor Antoni from his private clientèle; one case at the medical outpatient department; and finally one case at the neuro-surgical clinic. All these cases were personally examined by the author with the exception of those from Professor Antoni's private clientèle, where in one case I merely made a follow-up examination, and of one case from the nerve clinic, which I had no opportunity to follow personally.

Case histories:

Case No. 1. Nerve clinic; record 222/45. Man, aged 37. *History:* Previously the patient had practically always been healthy. On the 22nd Feb. 1945 he awoke at night—without preceding trauma or other known precipitating cause—with an

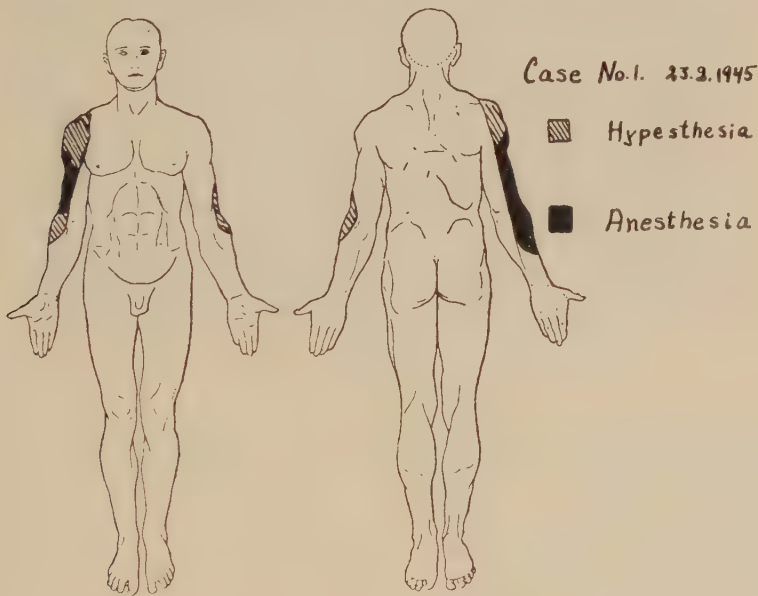


Fig. 1. Case No. 1.

The segmental distribution of sensory deficit (C 4/partly, C 5 and C 6/partly) suggests that lesion is in proximal components of the plexus.

intense pain in the right shoulder increasing with movements in the shoulder-joint. —The pain rapidly increased in intensity and after about half-an-hour it was almost unbearable; he also felt the skin to be numb in the lateral part of the right

upper arm. After 4 or 5 hours there was also pain in the left shoulder, though not so intense as in the right. On examination, soon after the onset, the following observations were made:—

Right shoulder: Capacity for movement: elevation outwards 30° , elevation forwards 45° .

Rotation greatly restricted.

Reports severe pain in the shoulder-joint on forced movements. Loss of sensibility in a palm-sized area over the deltoid muscle. Reflexes normal. Muscular force difficult to judge on account of the pain, but the deltoid and the outward rotators of the humerus are almost certainly paretic.—Because of the severe pain, the patient received an injection of 0.015 gm. morphine HCl, whereupon he had no pain for 6 hours. Afterwards the pain again became intense and he went to the outpatient department on the same evening. After another injection of 0.015 gm. morphine the pain subsided and did not recur until after 24 hours. After about a week no remaining pain.

Clinical examination 23.2.1945:

Motility in the right shoulder-joint: unable to abduct the arm, which hangs down limply. On attempts to adduct the arm, there is some muscular power, though apparently somewhat weaker than that of the left arm. Capacity for elevation: forwards 30° ; backwards: not possible. Outward and inward rotation somewhat restricted, with very weak muscular power. Right scapula: vertebral margin somewhat protruding. Motility in left shoulder-joint normal, though the muscular power here, too, seems to be somewhat impaired. The muscular force seems somewhat reduced in the hands (lack of prehensile power owing to pain?). Sensibility: see fig. 1. Muscle reflexes of the arms normal.

Roentgenograms of the right shoulder and cervical vertebrae: normal picture. *Duplography*¹: Free communication. Cerebrospinal fluid (CSF): normal findings.

In the course of about a month a marked atrophy of the right deltoid muscle and of mm. spinati occurred.

Since his discharge from the hospital in March 1945, the patient has been treated at the outpatient department with general physical therapy.

Follow-up examination in Feb. 1949: In the course of the two years immediately following the onset of the disease a slow but considerable improvement.

Clin. exam.: Slight atrophy of the right deltoid muscle and the right mm. spinati. Capacity for active movement in the affected shoulder-joint fairly satisfactory. Slight impairment of muscular power, especially abduction. Sensibility and reflexes satisfactory.

Case No. 2. O.P.D. for nervous diseases. Record 1186/46. Man, aged 34.

History: Previously quite healthy.

In Dec. 1945 the patient awoke in the night with intense pain in the left shoulder, radiating towards the nape and down the upper arm to the elbow. During the fortnight immediately following, the patient had every night 3 or 4 attacks of pain lasting from half-an-hour to one hour. The pain was described by the patient as "horrible". In the daytime milder ache of more continuous char-

¹ Measurement of the spinal fluid pressure on simultaneous lumbar and cisternal registration as well as Queckenstedt's test.

acter. When this fortnight had elapsed the nightly attacks of pain ceased; in the daytime, on the other hand, he had ache in the shoulder-joint, especially on movements; their severity, however, gradually abated.

About 3 weeks after the onset of the disease he noticed weakness in the left shoulder, with increasing atrophy of *mm. spinati*. This atrophy reached its culmination after about 3 or 4 months and has since then persisted.

Clin. exam. 17.4.46:

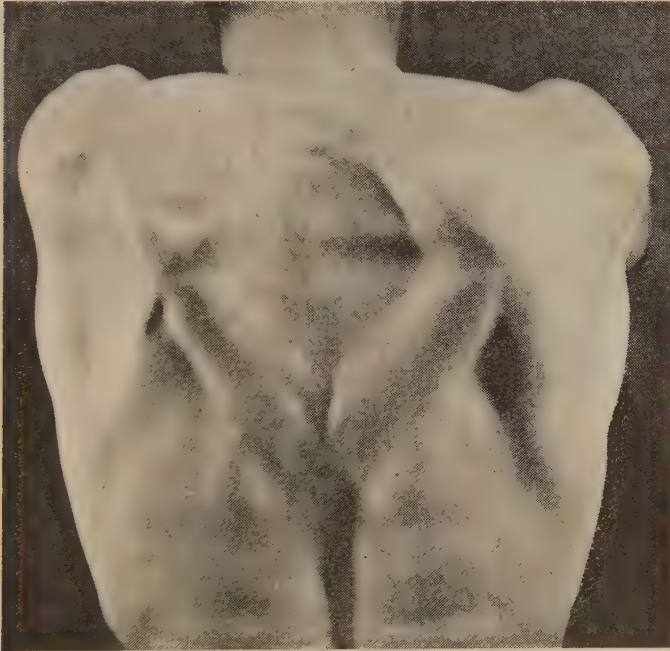


Fig. 2 Case No. 2.

Atrophy of *m. deltoideus* and *mm. spinati* on the left side.

Marked atrophy of the muscles in the fossa supra- and infrapinat. sin. Particularly in the fossa infrapinatus the muscles can scarcely be felt at all: the skin is taut over the scapula, and the bone can be palpated through the skin. Slight atrophy of the right deltoid, no weakness of the trapezius or serratus muscles. No impairment of movements in the right shoulder-joint. Muscular power greatly reduced on outward rotation and slightly reduced on abduction.

No disturbance of sensibility.

Reflexes: normal.

X-ray examination of the cervical vertebrae and the right shoulder-joint:
Normal conditions.

According to a communication from the patient in a letter, March 1949, the muscular power in the left shoulder had been gradually restored in the course of the two years following the onset of the disease.—Though, subjectively, a slight diminution of power still remains, the patient is now fully at work.

Case No. 3. Nerve clinic; record 1009/46. Man, aged 39.

History: Apart from an uncomplicated appendicectomy a fortnight before the onset of the disease, previously healthy.

In June 1946 the patient awoke at night with pain between the shoulder blades, radiating towards both arms and down the legs. The pain was rather severe, of a dull, boring character, and intensified by movements. It continued without intermission during the next four days, but then subsided.

On the second day of the disease the shoulder muscles were completely paralyzed. The arms hung down limply, the patient being unable to move them forwards, outwards, or backwards, or to rotate them in the shoulder-joint. He was able to flex the elbows, though even this required an effort. No diminution of force in the small muscles of the hand and fingers. After 2 days, however, some recession of the paresis was already noticeable.

On examination at a county hospital, 4 days after the onset, it was recorded

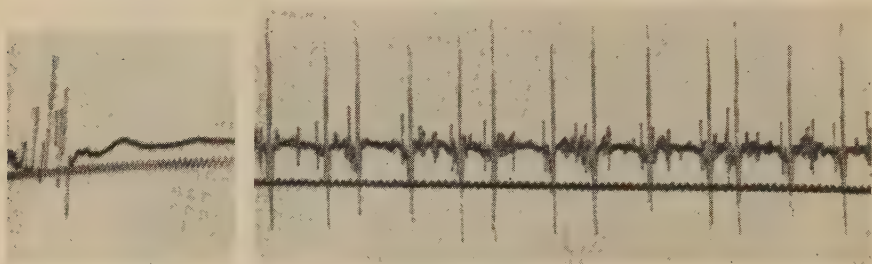


Fig. 3 Case No. 3.

Records from the deltoid muscle showing reinnervation activity. Numerous voluntary action potentials, mostly of small amplitude and with a duration of 2 msec and a number of polycyclic potentials.

that the patient could move the right arm 30° forward and the left arm to the horizontal plane. No disturbances of the reflexes.

In the course of the following month increasing atrophy of the deltoid on the right side and loss of sensibility over the upper lateral part of the deltoid (corresponding to the area supplied by the axillary nerve).

Examination of the CSF 7 weeks after the onset showed normal findings. He was treated with general physical therapy without appreciable effect.

In Nov. 1946 (5 months after the onset of the disease) the patient was admitted to the neurological clinic.

Clin. exam.: Marked atrophy of the right shoulder muscles especially of the deltoid and mm. spinati. Moderate atrophy of the left deltoid.

Motility: right shoulder-joint: abduction 20°.

 " " " : forward elevation 30°.

 left " " : abduction satisfactory.

Forward movement of supinated forearm: to the horizontal plane. Shoulder-joints free.

Sensibility: Over the right deltoid, over an area corresponding to the n. axillaris, loss of sensibility to pain and touch. Reflexes normal.

Roentgenogram of cervical and thoracic vertebrae: The intervertebral disc be-

tween C6 and C7 is somewhat lowered and on the edges of the corresponding vertebral bodies there are reactive exostoses both anteriorly and posteriorly.

CSF: Normal.

Myelogram with air: The subarachnoid space in the cervical and thoracic region shows normal findings.

Electromyography shows regeneration in the right deltoid muscle; normal findings as well as regeneration in the left deltoid.

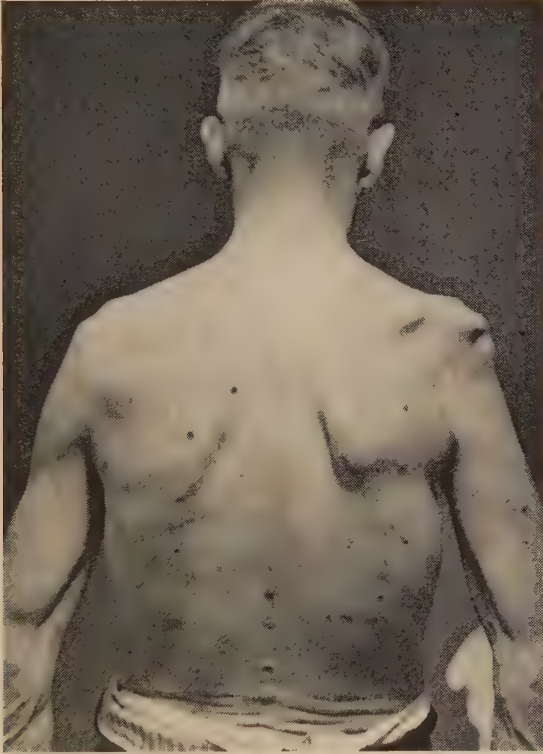


Fig. 4. Case No. 4.

The picture shows the atrophy of m. deltoideus and mm. spinati on the right side as well as a slight winglike position of the right scapula.

Clinical course: Improvement with general physical therapy plus abduction splint.

Follow-up examination in Feb. 1949:

Possibly a slight impairment of muscular power in the right deltoid; otherwise quite normal.

Case No. 4. Neurosurgical clinic; record 949/46. Man, aged 56.

History: Apart from attacks of asthma during the last two years, he had previously been healthy. While staying at a hospital in Stockholm for treatment of his asthma, the patient in the middle of May 1946 had a sudden onset of severe

pain in both shoulders; it was felt chiefly in the right shoulder and radiated down the right upper arm. At the same time he noticed a marked weakness in the right shoulder and arm and also numbness in the outer upper part of the arm. In the course of a few weeks a considerable atrophy of the deltoid and the mm. spinati developed on the right side.

The pain was most severe during the first week, but completely subsided after a month.

In the initial stage, besides inability to move the arm forwards or backwards or to abduct it at the shoulder-joint, the patient was unable to bend the elbow-joint. The ability to move the elbow-joint, however, was restored after a short time, whereas in other respects the patient's condition remained unchanged. The muscular power in the hands as well as that required for raising the shoulders was throughout satisfactory.

The patient was admitted to the clinic six months after the onset of the disease.

Clin. exam. in Nov. 1946:

Right shoulder: marked atrophy of the deltoid muscle and the mm. infra- and supraspinatus. The biceps brachii m. on the right side is possibly somewhat more flaccid than that on the left. No measurable biceps atrophy. Slightly winglike position of the right scapula. Motility in the right shoulder-joint: Abduction: 0.

Forward and backward movement: slight.

Left shoulder-joint: satisfactory.

Capacity for passive movement in the right shoulder-joint: The arm can be lifted merely to the horizontal plane, a movement followed by intense pain.

Sensibility: Within a palm-sized area in the lateral range of the upper arm the sensibility to all kinds of stimuli is reduced.

Reflexes: normal.

Roentgenogram of cervical vertebrae: large projecting exostoses, constricting the intervertebral spaces C5-C7.

Roentgenogram of right shoulder: decalcification in caput humeri.

Myelogram with air: nothing noteworthy. CSF: normal. Electric stimulation: degeneration reaction of m. deltoideus dx.

Follow-up examination in Feb. 1949: Subjectively some improvement in the course of the year 1947; since then no change.

Clin. exam.: As before, marked atrophy of mm. deltoideus, supra- and infra-spinatus as well as slightly winglike position of the scapula on the right side. No capacity for abduction. Forward and backward arm movements ca. 30°. Slight loss of sensibility to stimuli of all kinds within the upper lateral range of the right upper arm.

Electromyography: Merely a few spontaneous fibrillations: no voluntary activity. Advanced stage of injury to the peripheral neuron.

Case No. 5. K. V. E. Man, aged 54.

Apart from high blood pressure, which was noted at a medical examination 11 years before, he had been quite healthy.

In March 1943 he had a sudden onset of severe pain in the left shoulder and arm, with concomitant weakness in that shoulder and upper arm. Received x-ray treatment of the left shoulder and was restored after about a fortnight.

In April 1948 a sudden onset of intense pain in the right shoulder and upper arm followed on the 4th day by paralysis. Abduction at the shoulder-joint and

flexion of the right elbow was impossible. The pain, however, gradually subsided in the course of the following fortnight, after which it ceased entirely. The paralysis diminished in about a week, after which the muscular power was slowly restored.

Clin. exam. in Dec. 1948:

Slight paralysis in the deltoid and biceps brachii on the right side. Sensibility normal. The right biceps reflex weaker than the left. Slight peri-omarthrititis in the left shoulder. Blood pressure 220/110. Physical condition otherwise normal.

Electromyography: Injury of the peripheral nerve.

Case No. 6. H. S. Man, aged 64.

In the middle of March 1945 for about a fortnight he had a "sore throat"; during this time, however, he was up, attending to his work.

A day or two after the patient had felt quite restored from the throat infection, he awoke at night with a sudden attack of intense pain between the shoulder-blades, radiating down both arms out to the index-fingers. The pain was very intense for about ten days, but gradually abated and had ceased after a month. Immediately after the onset of pain, he found that both index-fingers were very weak and could scarcely be flexed.—Whether there had been any weakness in the shoulder muscles during the first week the patient was unable to state, as he had gone about in a perpetual morphine "intoxication" because of the otherwise unbearable pain.—No weakness in the shoulder-girdle has subsequently occurred.

Clin. exam. in April 1945:

Physical condition: Blood pressure 195/100; otherwise normal.

Neurologically: Unable to flex the outer phalanges of either index-fingers; otherwise normal.

In the course of the next few months ability to flex the right index-finger was recovered, whereas the condition of the left index-finger remained unchanged.

Follow-up examination in Feb. 1949: Neurologically: Slight weakness in flexing the outer phalanx of the right index-finger. Inability to flex the outer phalanx of the left index-finger.

Sensibility: Slight loss of sensibility over both index-fingers. Neurologically in other respects normal findings.

Case No. 7. Nerve clinic; record 876/1948. Man, aged 65.

Case history: Apart from bronchiectases, for which he had been treated several times in hospital during the years 1943-1947, and gastric ulcer 1945-1947, he had been healthy. At the time of the onset no gastric trouble and very slight trouble from the bronchiectases. In the middle of September 1948 the patient awoke at night with violent, continuous ache in the right shoulder, most marked over the right deltoid. The pain was not radiating, but was aggravated by the slightest movement. The patient held his arm pressed to the side, with the forearm bent. He does not know, therefore, whether there was then any weakness in the shoulder-joint. The pain abated after about 3 days; he then noticed that he could not lift his arm forwards or outwards. In the course of the following weeks atrophy of the deltoid and the mm. supra- and infraspinatus supervened, as well as a slightly winglike position of the right scapula. The patient came to this hospital for examination 2 months after the onset.

Clin. exam. in Nov. 1948:

General condition not affected, though patient somewhat emaciated. Pulmonary

rales heard bilaterally. Blood count: hb 68, red cells 3.38 million. Sedimentation rate 48 mm/1 hr. Afebrile.

Neurologically: right shoulder: marked atrophy of the deltoid and the mm. supra- and infraspinatus. Slightly winglike position of right scapula. Motility almost completely lacking in the right shoulder-joint, whereas the muscular power in the elbow and hand is normal. Some weakness in retracting the shoulder, indicating that the rhomboid muscle on the right side had also been involved. Sensibility and reflexes normal.

Roentgenogram of cervical vertebrae: the discs between C V-VI and C VI-VII greatly reduced in height, besides deforming exostoses anteriorly and posteriorly.

Roentgenogram of right shoulder-joint: normal.

Duplography: normal. CSF: normal.

Electromyography: grave injury to the peripheral motor neuron, with denervation.

Case No. 8. Medical O.P.D., K. G. K. Man, aged 45.

Case history: Previously healthy. Fell ill at the beginning of March 1949 with an infection of the nasal cavities and fever (no sulpha-treatment). A few days after his recovery from the infection, the patient had an attack of intense pain in the left part of the neck, radiating down to the supraspinous fossa and over the deltoid. The pain was continuous and lasted for two days. About the same time as the pain subsided, paralysis in the left shoulder supervened; on the other hand, no noticeable weakness in the forearm and hand.

Clin. exam. in April 1949 (about 5 weeks after the onset):

Left shoulder: moderate atrophy of the deltoid and the mm. supra- and infraspinatus. Motility: abduction 30°, forward elevation 30°, retraction 40°. Range of movement slightly restricted on rotation in the shoulder-joint. Motility of the left elbow-joint normal. Slight impairment of the muscular power needed for flexion. Sensibility: normal. Reflexes: biceps somewhat weaker on the left side, otherwise normal.

Roentgenograms of cervical vertebrae: The discs between C IV-V and C VI-VII moderately reduced in height and surrounded by small reactive exostoses. On a level with the disc between C VI and VII they bulge rather deeply into the corresponding intervertebral cavities on either side.

Roentgenograms of shoulder-joints: normal.

Electromyography: Peripheral lesion of the motor neuron, with partial denervation.

DISCUSSION. ANALYSIS OF THE CASES

The material consists solely of men between the ages of 34 and 65 years, corresponding to an average age of about 49.

In none of the cases reported here the onset had been preceded by serum or vaccine therapy. There was no known precipitating cause. In one of the cases (No. 3) the patient a fortnight before the onset had an uncomplicated appendicectomy, in another case (No. 4) the patient was being treated at a hospital for a mild asthma at the

time of the onset, whilst in cases Nos. 6 and 8 the onset of the disease had been immediately preceded by an infection of the throat and the nasal cavities.—In none of the cases under review was there any record of headache, stiff neck, or rise of temperature.

The onset of the disease in all the cases had been very dramatic, with a sudden attack of violent pain. Paralysis as a rule supervened in the course of the first few days and was most severe in the initial stage. In case No. 2, however, about three weeks elapsed before paralysis appeared. In three cases only the right shoulder was affected. In two cases the affection was bilateral, but asymmetric. In cases Nos. 4, 5, and 8 the elbow flexors were also initially involved. In case No. 6 the flexor digitorum profundus was partially affected bilaterally.

In 4 cases there were disturbances of sensibility, the commonest type corresponding to the area supplied by the axillary nerve. In case No. 1 it was particularly marked (see Fig. 1), and in case No. 6 there was a slight numbness of both index-fingers. In 6 cases muscle atrophy supervened very rapidly and was generally pronounced. In case No. 5 the atrophy of *m. biceps brachii* and *m. deltoideus* was moderate; in case No. 6 there was no atrophy.

It was often difficult to determine in what part of its course the nerve was injured, *i.e.* whether the peripheral part only, the plexus or the roots had been affected.

The nerves affected were almost invariably derived from C5 to C6, the frequency being the following.—

n. axillaris	7
n. suprascapularis	6
n. thoracalis longus	5
n. musculocutaneus	3
n. dorsalis scapulae	1
n. medianus	1

In all the cases examined (4 cases) investigations of the CSF showed normal conditions.

Roentgenograms of the vertebrae revealed spondylosis deformans of the cervical vertebrae in four cases, in three of them also disc degeneration.

Myelograms with air were done in two cases: normal findings.

Electromyograms showed injury to the peripheral motor neuron, leading to denervation of the muscle.

Treatment and prognosis.

In addition to general physical treatment, the affected arm in the cases showing a marked atrophy of the deltoid had been placed in an abduction splint. This seems to be an important feature in the treatment, where it is desired to avoid stretching an already very weak muscle.

The prognosis, which has been stated in the literature to be rather bad as regards the restoration of function, has been found, on the contrary, during a sufficiently long period of observation to be rather good. Merely in one case (No. 4) the atrophies after an observation period of $2\frac{1}{2}$ years were still found to be very pronounced, Cases 1-3, where the atrophies had at first been very marked, have in the course of 2 years shown a surprisingly satisfactory restitution. Case No. 5 has shown a moderate improvement; as regards cases Nos. 5, 7, and 8, the observation period is still too short to judge the final result.

Differential diagnosis.

1. "*Serum neuritis*". Neurological complications as sequelae to serum injection have been described by several authors (Allen, Doyle, Antoni, Thaon, Kennedy, Smith, Thompson, and others). The complaint as a rule sets in 7-10 days after the serum injection, usually with severe pain interscapularly and in the upper arms, frequently preceded by various symptoms of serum disease. The pain persists for several days to a week or so and is followed by paralysis in muscles innervated from C5 and C6, sometimes merely by paralysis of the serratus magnus muscle or the deltoid.— The features of this disease are identical with the shoulder-girdle syndrome and can be distinguished from the latter only by knowledge of a preceding serum injection.

2. *Acute poliomyelitis*. In view of the absence of fever, meningeal symptoms, hyperesthesia, and in most cases the existence of symptoms of anesthesia, poliomyelitis may be ruled out as a possible diagnosis in the cases reported here.— During the acute stage of the disease, the CSF was examined merely in one of the cases, where the findings were normal.— Apart from the neurological symptoms in the upper extremities, the neurological status was normal also in other respects.

3. *Herniated cervical discs*. Prolapse of the cervical intervertebral discs has been reported in the course of the last few years by a number of authors (Spurling and Scoville 1944, Elliott and Kremer 1945, Sahlgren 1946, Frykholm 1947). In these cases also the pain

may have a sudden onset and occasionally be very intense; often, however, the pain is less severe, though it tends to persist over a prolonged space of time. As a rule merely one root is affected—usually C7.—If paralysis occurs, it often develops more slowly, and is not often rapidly followed by pronounced atrophy. The same remarks apply to dura-sheath strictures round cervical roots (Frykholm).

4. "*Brachialis neuritis*" or "*brachialgia*". This diagnosis includes several conditions; it is only quite recently that cervical disc prolapses have been differentiated. In these cases also the pain may occasionally be sudden and intense; it may moreover be attended by slight general impairment of muscular power, with diffuse sensory disturbances and often with weakened muscular reflexes.—Localized paralysis with pronounced atrophy does not occur in these cases.

5. *Progressive muscular atrophy*. Here the differentiation is easy. The acute onset with pain, the rapidly supervening atrophy, the absence of fascicular twitches, the nonprogressive course and the rather frequently occurring disturbances of sensibility are features that completely distinguish it from progressive muscular atrophy.

6. Finally, the possible occurrence of *polyradiculitis of the Guillain-Barré type*, of *syringomyelia*, or of *periarteritis nodosa* should be considered from the viewpoint of differential diagnosis. In none of the above-mentioned cases have these diagnoses been found justified.—In the initial acute stage intrathoracic conditions of pain should also be considered. I have observed a couple of cases beginning with a very acute onset of intense interscapular pain radiating towards the left shoulder; special investigations, however, showed in the one case a minor spontaneous pneumothorax on the left side, in the other a "dissecting" aortic aneurysma.

ETIOLOGY

The pathogenesis as also the pathologico-anatomical picture in these cases still remain to be made clear.

The resemblance to "serum-neuritis" is indeed rather striking. The most generally adopted explanation of this latter condition is an allergically developed perineural edema in the affected roots or nerves. Certain authors (such as Hughes) have pointed out—but not proved—the possibility of a virus infection even in cases of "serum-neuritis". In such cases the virus is supposed to have followed along with the needle in the serum injection. There have also been speculations on

the possibility of a primary affection of the nutrient vessels of the nerves themselves, with resulting thrombosis of the vessel and infarction of the nerve. This view has been stressed particularly by Weinstein, who parallels it with multiple neuritis in cases of periarteritis nodosa. In these last-mentioned cases light has been thrown on the pathology especially by Kernohan and Woltman, who have shown that neural infarction had occurred.

The large reports on casuistics are concerned mainly with military personnel subjected to vaccination or protective inoculation of different kinds. In more than half of the cases the onset had been preceded by an infectious disease and had usually occurred while the patient had been convalescent. An allergic factor as a precipitating cause seems therefore to be rather probable, though a virus infection cannot be excluded.

NOMENCLATURE

As may be seen from the introduction, a number of different names have been proposed for this group of diseases.

As the pathogenesis is still unknown, descriptive diagnoses have as a rule been given. Such diagnoses, however, are apt to be cumbersome; the term "acute shoulder neuritis" has accordingly been preferred.

SUMMARY

Eight cases of a shoulder-girdle syndrome attended by muscular atrophy are described. In none of the cases had serum been given before the onset.

The syndrome is characterized by a sudden onset of intense pain in the affected shoulder, soon afterwards followed by paralysis in different shoulder muscles, usually *mm. spinati* and the deltoid. The pain subsides after a few days to a few weeks. Very marked atrophies develop in the course of the next few weeks after the onset of the disease. Within a period of about two years from the onset a satisfactory restoration has generally been observed. The pathogenesis is still unknown, but is probably due to an allergic condition, though a virus infection cannot be excluded. Similar cases have previously been very rare, but since 1942, according to Burnard and Fox, about 200 cases have been reported in Anglo-American literature.

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DIFFERENT MIXTURES OF SYNTONIC AND ASTHENIC PERSONALITY TRAITS

An Experimental Study

By

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The examination of a patient suffering from a mild mental disorder should not only seek to define the clinical picture as obsessions, delusions, depression, anxiety state, or the like. It should also attempt to determine the basic personality type of the patient. Doing so greatly facilitates the classification, diagnosis, and treatment of the case. Little is gained, however, by the use of such terms as neurotic or psychopathic for the definition of the personality. Adjectives like syntonic, psychasthenic (or asthenic) or hysterical give much more information. Sjöbring considers these three basic types of personality and genuine intellectual inferiority to be minus variants of four constitutional factors.

These factors he calls validity (V), stability (St), solidity (So) and capacity (K). Thus he uses the term subvalidity for constitutional asthenia, substability for constitutional syntonía, subsolidity for constitutional hysteria and subcapacity for constitutional intellectual inferiority. The outstanding feature of the Sjöbring psychological system is the uniform theoretical point of departure, the dynamic, functional basis for the explanation of all these psychological variants, the variations of which are deducible from a general hypothesis. The variants are considered as phenomena within different functional areas which vary independently of one another from one biological disposition to another. A person may be both substable and subvalid, he may have minus functions of all four factors or he may have a plus function of one or more. Accordingly, the theory allows for many combinations of the variants.

Sjöbring's theory, correct or incorrect, has led to attempts to use compound definitions of personality. Compound definitions of this kind are very useful in clinical work and also provide an excellent basis for research in experimental psychology. Thus, instead of speaking only of hysterical, asthenic, and syntonic personalities, it has proved practical and more in keeping with facts also to use terms

such as hystero-asthenic, asthenosyntonic and hystero-asthenosyntonic for a description of the personality.

The present paper deals with an experimental study on personality variants with different degrees of asthenic and syntonic traits.

The investigations were carried out at the Psychiatric Department of the Sahlgren's Hospital in Gothenburg. All the subjects were examined according to a questionnaire which, among other things, brought out any of the main features of the asthenic and syntonic personalities. The traits considered to make up the asthenic personality about correspond with those described by Janet. (Janet's account is also the main basis of Sjöbring's further analysis of the asthenic personality.)

Accordingly, the following traits were considered to be *asthenic*: carefulness, excessive orderliness, preciseness, pedantry, hyperconscientiousness over trifling details, vacillation and indecision, constant checking up, sense of insecurity, retiring disposition, tenseness in the presence of persons in superior standing and in new situations, worry over any little departure from the customary routine, inclination to feel rushed and harassed and liability to fatigue.

The two main features of the *syntonic* personality, in the sense of Bleuler, are the ones which Kretschmer described as characterizing the cyclothymic personality, viz. warmth and firm contact with the reality around them. The syntonic traits include: sociability, facility in striking up an acquaintance and making friends, ready sympathy, strong reactions to sources of pleasure or displeasure, emotional attitude towards nature, practical disposition, tendency to spontaneous changes of mood "for no obvious reason", and inclination to describe themselves as creatures of emotion.

The patients were naturally asked a large number of other questions than the ones in the questionnaire, depending on their personal make-up and any special problems involved. The diagnosis of the personality, however, was made primarily on the foregoing principles.

In an earlier study with my ring test¹ I observed that patients diagnosed as substable, or what is herein called syntonic, had the highest percentage of initial colour answers (RCi) and the subvalid (asthenic) group the lowest percentage. Cases with both substable and subvalid traits showed an intermediate value. The figures were significant and the same results were obtained from two series from two different hospitals. Although the investigations clearly showed that the syntonic personality tended towards a high colour percentage and the asthenic towards a low one, the nature of this relation was

not then clear. I presumed, however, that there were two positive attitudes, one a colour attitude represented by the substable (syntonic) persons and the other a non-colour or form attitude represented by the subvalid (asthenic) persons. The fact that the substable-subvalid (asthenosyntonic) persons took an intermediate position in all forms of grouping could be attributed to competition between the two factors, one of which favours the colour attitude and the other the non-colour attitude.

The present study was carried out, amongst other reasons, in order further to elucidate the apparent antagonism of the syntonic and asthenic attitude in the "ring test". It also aims at showing that the asthenosyntonic personality can be classed in several mixed types, not only for clinical purposes but also for research in experimental psychology.

The series includes 300 adult patients suffering from mild mental illnesses, e.g., mild depression, compulsive and obsessional states, sleep disorders and hysterical disorders, thus complaints which many would classify as neurotic conditions. Some of the patients, 155 in number, were examined while staying in the Psychiatric Department. The others, amounting to 145, were taken from my private practice. The personality was analyzed before the experimental examination in each case, and the results noted before the testing was done.

The series was divided according to the personality analysis into five groups ranging from the pure syntonic to the pure psychasthenic. (The strength of the syntonic and asthenic factors was graded on the basis of Sjöbring's terminology. Thus 5 and higher figures denote the absence of a minus function of the respective variant, 4 a moderate minus variation and 3 a marked minus variation.)

The five groups were characterized as follows:

Syntonic (St_3V_5), abbreviated to S,

Syntonico-asthenic, in which syntonic traits dominated (St_3V_4), abbreviated to SA,

Cases with the two features equally pronounced (St_3V_3 , St_4V_4), abbreviated to S=A,

Asthenosyntonic, in which asthenic traits dominated (St_4V_3), abbreviated to AS, and

Pure asthenic (St_5V_3), abbreviated to A.

(The small uncertain groups St_5V_5 and St_5V_4 , altogether 11 cases, are excluded).

Examination with the Ring Test.

The ring test^{1 2} uses two cards each of which contains the picture of a ring. One of the rings is red and the other blue and the two also

differ in various ways as regards shape, location and other details. The subject is given the cards with the following instructions: "Here you have two rings. They are not alike, as you see. In what ways do they differ?" Initial colour responses, i.e., a comment on the difference in colour in the first or second answer, are abbreviated as RCi.

The personality diagnosis of the lying-in patients was made in cooperation with the assistant physician for the respective ward. I alone was responsible for the diagnosis of the out-patients. Although the two groups were of about the same composition and I was wholly or partly responsible for the diagnosis in both cases, I first made a comparison between the two series.

My investigations of 1938 having revealed such a slight difference between the results of the men and women, I did not bother to differentiate between the sexes in this study.

TABLE 1
Distribution of RCi % among in- and out-patients.

	S	SA	S=A	AS	A
In-patients	87.1	64	36.7	31.8	14.3
Out-patients	90.9	65.7	43.2	35.3	9.1

The results from the in- and out-patients are seen in *Table 1*. This table shows that there was very little difference between the two groups. I felt justified, therefore, in treating the two categories as one series.

The results of the ring test in the whole series are shown in *Table 2*. It is seen there that the RCi percentage is highest among the purely syntonic cases and lowest among the purely asthenic ones, and decreases successively as the syntonic traits diminish and the asthenic ones increase. The differences between S and S=A and S=A and A are statistically significant, amounting to 49.5 ± 6.6 and 26.2 ± 8.6 per cent., respectively.

TABLE 2
Distribution of RCi % in different personality variants.

	S	S A	S = A	A S	A
N	(53)	(60)	(97)	(56)	(23)
RCi %	88.7	65.0	39.2	33.9	13.0

The syntonic factor was of equal strength in the two first groups, the only difference between them consisting of the admixture of asthenic features in the second group. The difference between their RCi percentages, however, was significant, amounting to 23 ± 7.5 per cent. This fact gives further support to the assumption that it is the asthenic factor which lowers the tendency towards colour reactions. This assumption is also borne out by the consistent statistical tendency which distinguishes the table as a whole, as well as by a comparison between the groups SA and the part of the S=A group containing St.V. The latter group includes 76 cases and its RCi percentage is 39.5 per cent. The difference between these groups, which contain about an equal amount of syntonic features, is statistically significant, amounting to 25.8 ± 8.3 per cent. The only difference between the groups as regards personality is that one contains a stronger asthenic factor, and this was the one with the fewer colour responses.

Study with the ring test, accordingly, shows that the percentage of initial colour answers increases with an increase in the syntonic factor and decreases with an increase in the asthenic factor.

I have discussed in other papers (1, 2, 3, 4) the nature of the colour reaction and its psychological meaning. Although some persons immediately comment on the difference in colour and others never mention it, we cannot be sure that it is colour as such that causes the difference in response. The correlation between the results of the ring and sorting test would indicate that there is a common attitude,—a colour attitude. This attitude, however, might be explained by other factors than attraction to or interest in colours. As I have pointed out, many of the various perceptual types formulated seem to represent similar contrasting pairs, e.g. analytic and synthetic types and discrete and total types. Müller-Freienfels (5) distinguishes between one type which primarily sees details and particulars and has his attention directed towards the special case with its peculiar features and another type characterized by a more comprehensive conceptual attitude in the relevant mental processes. Peters (6) speaks of a "leptic" attitude, that is, a more passive attitude towards that observed, and a "ctetic", active attitude. The impressions yield themselves to the former type, but are made the object of an investigatory process in the latter case.

There is reason to believe that the synthetic, total, passive attitude is connected with a colour attitude, and the analytic, discrete, active perception with the non-colour or form attitude. It seems to be a question of totality versus particulars, the colour attitude representing the holistic, synthetic point of view and the form attitude the piecemeal, analytic point of view.

Examination with the Text Test¹.

In order further to study this question, I constructed a new test, the *text test*. The subject is given a paper containing versions of a well known proverb. One version reads: "A bird in the hand is worth two in the bush" (*Bättre en fågel i handen än tio i skogen*). The other reads: "A fowl in hand is worth three in the bush" (*Hellre en fågel i hand än tolv i skogen*). The first version is typewritten and the second is handwritten in the same black colour below. The instructions given are as similar as possible to those used in the ring test: "Here you have two texts. They are not alike, as you see. In what ways do they differ?"

Some persons begin by calling attention to the different types of writing (style reaction). Others immediately go into the differences in the formulation of the proverb (word reaction).

In a comparative investigation (4) I showed that there was a close connection between the results of the ring and text test. Thus the colour reactors in the ring test contained a greater number of style reactors in the text test than the form reactors. Similarly, the persons who first mentioned the difference in writing in the text test contained a greater percentage of colour reactions in the ring test than the group with word reactions.

In order to study the results of the text test in the different personality groups in question, the present subjects were also given the text test. The two tests were given in immediate succession, with the ring test first in each case.

The connection previously observed between the results of the two tests was also observed in the present, entirely different series. Thus 101 out of 153, or 66.0 per cent., of the colour reactors in the ring test were style reactors in the text test. The corresponding figures for the form reactors were 68 out of 147, or 46.3 per cent. The difference, 19.7 ± 6.0 per cent., amounts to 3.3 times the standard error. Furthermore, 101 out of 169 style reactors in the text test, or 59.8 per cent., had RCi responses and 52 out of 131, or 39.7 per cent., of the word reactors. The difference, 20 ± 5.7 per cent., amounts to 3.5 times the standard error.

This correlation having been established, it is not surprising to find that the style reactors in the text test showed the same distribution among the different personality groups as the colour reactors.

Table 3 shows the results of the text test. It is seen there that

¹ The Text Test (in English or Swedish) and the Ring Test can be obtained from the author.

TABLE 3

Distribution of style answer % in different personality variants, examined with the text test.

	S	S A	S = A	A S	A
N	(53)	(60)	(97)	(56)	(23)
Style answer %	83.0	58.3	57.8	43.0	30.4

the percentage of style reactions decreases in the same way as the RCi responses as the groups pass from the purely syntonic to the purely asthenic. The difference between the two extremes is 53.4 ± 10.9 per cent. The difference between the S and S=A group is 27.4 ± 7.2 per cent., thus 3.8 times the standard error, and between S=A and A 27.4 ± 10.8 per cent., or 2.5 times the standard error. The two first groups, where the syntonic factor was supposed to be of equal strength, showed a statistically significant difference, 24.7 ± 8.2 per cent., as in the ring test. This difference must have been due to the addition of an asthenic factor to the second group. The differences between the other adjacent groups are not significant, but the figures strongly indicate that the syntonic factor favours style responses and the asthenic factor word responses.

Combined Results of the Ring and Text Test.

We have now seen that the two tests give similar results, though the ring test brings out more pronounced differences between the different personality mixtures. It would be interesting, therefore,

TABLE 4

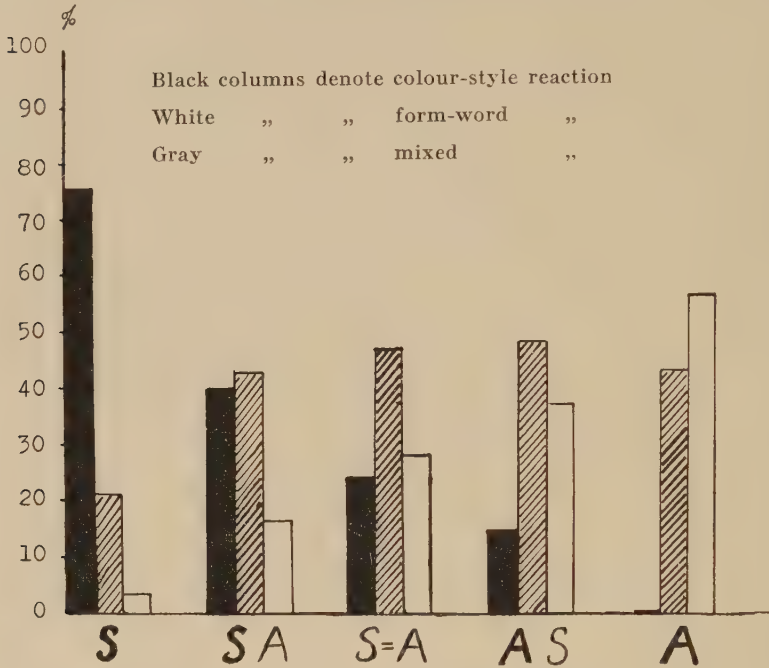
Results from the combined ring-text-testing.

	S	S A	S = A	A S	A
N	(53)	(60)	(97)	(56)	(23)
Colour style %	75.5	40.0	24.7	14.3	0
Form word %	3.8	16.7	27.8	37.5	56.5
Mixed	21.7	43.3	47.5	48.2	43.5

to study the combined results of the two tests in the different personality groups in question. We then have three possibilities: (1) colour answers in the ring test and style answers in the text test, (2) non-colour answers in the ring test and word answers in the text test, and (3) mixed answers, i.e., colour-word or form-style reactions. *Table*

Figure 1.

Distribution in different personality mixtures of the reactions in the combined ring-text-testing.



4 shows the distribution of the colour-style, form-word and mixed reactions in the different personality groups.

It is seen from this table and even more clearly from *figure 1* that the colour-style reactions dominate in the purely syntonic subjects and decrease gradually with an increasing admixture of asthenic traits, disappearing entirely in the purely asthenic category. The figures form a statistically significant curve, as seen from the combined values in *Table 5*.

TABLE 5

Difference between the percentage values in different personality mixtures.

	Diff.	Diff/ ϵ Diff.
Colour style %	S — S=A = 50.8 ± 7.5	6.8
	S=A — A = 24.7 ± 6.2	4.0
	SA — AS = 25.7 ± 7.9	3.2
Form word %	S — S=A = $\div 24.0 \pm 5.3$	4.5
	S=A — A = $\div 28.7 \pm 11.3$	2.5
	SA — AS = $\div 20.8 \pm 8.1$	2.6

As might be expected, the form-word responses increase with increasing strength in the asthenic factor. They are minimum in number at the syntonic pole and maximum at the asthenic pole. Accordingly, combining the results bears out the separate test results and indicates that there is a distinct antagonism between syntonia and asthenia as regards the results of the two psychological tests.

Thus asthenic and syntonic factors seem to play tug-of-war in this respect and, judging from the results of this study, each appears to have an equally strong pull. The answers in the group in which the two factors are about equally balanced, $S = A$, are distributed almost exactly according to the curve of random distribution. Instead of the theoretical 25 per cent. colour-style, 25 per cent. form-word and 50 per cent. mixed answers, we get 24.7, 27.8 and 47.5 per cent., respectively. A larger series is needed, however, to confirm the amazing symmetry of this distribution.

These experiments have thus confirmed our clinical experience that syntonic and asthenic features often occur side by side in the same subject and in different proportions from person to person. Examination with the ring and text test is of theoretical importance, therefore, as it may be used for experimental studies of personality. A combination of these tests will probably also prove of practical and diagnostic value. If we have a patient judged from clinical examination to be purely syntonic, according to the present figures the chances are at the most 10 per cent. (3.8 ± 2.6 per cent.) that he gives form-word answers. If we have a patient considered to be purely asthenic, the chances are at the most 10 per cent. that he gives a colour-style response.

For safety's sake, however, one should make certain that the patient does not suffer from intellectual inferiority. Only a few of the present subjects had an intelligence below normal and the influence of the intelligence factor, therefore, could not be judged from this series.

I pointed out earlier that the results of the ring test were little influenced, if at all, by hysterical traits (variations in Sjöbring's solidity factor). Examination of the $S = A$ group showed that the subjects with hysterical features did not react differently from the ones without, the results being about the same in both the ring and text test.

While these experimental results point to the occurrence of well-defined personality traits of an asthenic, asthenosyntonic or syntonic character, they say nothing, of course, as to whether the traits are constitutional or of more superficial origin. The results of the ring

test are connected to a certain degree with certain physiques, as I pointed out previously¹. Thus the most pyknic persons have the highest percentage of colour answers and the most leptosomatic the lowest percentage. I determined the body type with Strömngren's index in this study, too, but only with 154 of the hospitalized patients. The physiques of these patients are shown in *Table 6*. A plus index means a pyknic constitution and a minus index a leptosomatic build. Although, according to Strömngren himself, the zero point seems to lie a little way in on the minus side, I grouped the cases with ± 0 as neutral in this small series, particularly as I had used this procedure formerly.

TABLE 6
Experimental findings in different body types
(according to Strömngren's index).

Index		+	± 0	—	Diff.	Diff./ ϵ Diff.
N		23	4	127		
Ring	Colour	65.2 0/0		47.2 0/0	18.0 ± 10.86 0/0	1.7
Text	Style	78.3 0/0		58.3 0/0	20.0 ± 9.64 0/0	2.1
Ring-Text	Colour-style	47.8 0/0		32.3 0/0	15.5 ± 13.76 0/0	1.1
Ring-Text	Form-word	4.3 0/0		24.4 0/0	20.1 ± 5.69 0/0	3.5

This table bears out the assumption previously reported that a pyknic build favours colour reaction and a leptosomatic build non-colour reaction. While this small series did not reveal a significant correlation between the body type and the separate results of the ring and the text test, presumably colour and style answers dominate in the pyknic subjects. As regards the combined test results, the pyknic subjects had the least number of form-word responses and the largest amount of colour-style responses. The difference between the frequencies of form-word reactions in the pyknic and leptosomatic groups was significant, amounting to 3.5 times the standard error.

It may be said, therefore, that the examination indicates that constitutional factors, in so far as they are shown by Strömngren's

index, play at least some part in the individual's reaction to the ring and text test, especially as regards the combined results.

It is possible that this may only be due to the well known fact that syntonic people are apt to have a pyknic build. No conclusions regarding an affinity between a psychasthenic attitude and leptosomatic build can be drawn from the present figures.

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A FAMILIAL EXTRA-PYRAMIDAL SYNDROME

By

OTTAR LINGJÆRDE and HANS KVADSHEIM

Heredofamilial and degenerative diseases of the nervous system manifest themselves through a strongly varied symptomatology. But there are certain characteristic features. Firstly, most of the victims of these diseases are normal at birth. When the symptoms appear, they practically always make slow progress. As the beginning is so insidious, it is practically never possible to state accurately when the first symptoms appeared. The diseases usually commence at the same age in the generation concerned. A traceable hereditary affliction is not always present. As the etiology is uncertain we operate with hypotheses like abiotrophy and hereditary disturbances of the metabolism.

It is hard to classify these diseases because the symptoms are so infinitely varied. Therefore we cannot go beyond speaking of more or less well defined syndromes, many of which possibly represent different degrees of the same abnormality.

Since the end of the 19th century a number of articles have been published on extra-pyramidal syndromes which frequently bear the names of the various authors. In some cases accurate pathologico-anatomical studies have been made. In 1920 C. & O. Vogt gave a detailed description of 33 cases showing striate symptoms. Here a distinction is made between *État marbré*, presumably caused by germinal damage and situated in the corpus striatum, and an *État démyélinique* situated in the globus pallidus and with demyelination as a particularly conspicuous change. The cases described begin with a general muscular rigidity, later involuntary movements of the athetoid type. In some of the cases intense and painful spasms with bendings and stretchings of the extremities appeared. The patients died between the ages of 5 and 15 years.

In 1922 Spatz & Hallervorden described a family of 12 children, 5 of whom suffered from the same disease, while 2 of the others

were in an insane asylum. The disease began between the ages of 7 and 9 years and death occurred when they were about 22. In these cases there was rigidity of the legs, but athetoid movements were observed only in one of the cases. The speech was always affected. The children were debile from birth, and during the course of the disease they were demented. Pathologico-anatomical examinations showed pigmentary degeneration of the globus pallidus and substantia nigra.

Kalinowsky mentions a family with 4 children, 3 of whom became ill at 9 to 10 years of age. In these both arms and legs were affected. Athetosis appeared only in one case, and in this it was bilateral; the two others were subjected to rhythmic tremors of a Parkinsonian type. The children finally became helpless, their legs stiffened in a bent position by spasms. They died demented. Pathologico-anatomical examinations showed changes of the same kind as in the cases reported by *Spatz & Hallervorden*. Therefore the disease was classed in the same group.

Winkelmann mentions two brothers who became night-blind at the age of 3 to 4 years because of pigmentary degeneration of the retina. At 12 they were blind and showed muscular rigidity of the extra pyramidal type. There were no involuntary movements. Pathologico-anatomical examinations showed the same changes as those described by *Spatz & Hallervorden*.

As these diseases are comparatively rare and the combination of symptoms so varying, a disease particularly rich in symptoms described as early as 1830 by district physician *P. Jensen*, Ålesund, Norway, may be of interest. The article was published in "Eyr" in 1832, Vol. 7, p. 1. It deals with a family of 6 children, 4 of whom suffered from the same disease. Nothing is mentioned of hereditary affliction.

When the district physician examined the family 2 boys were dead respectively 5 and 3 years previously, both at an age of 9 years. A third child, a girl, died shortly after, also 9 years old, and a post mortem examination was made by the district physician. A fourth child, a girl, was at that time 7 years of age and showed the same symptoms as the deceased. The ages of the two healthy children were 4 years and 1 year.

We see from the description that all children were healthy and thriving until they were about to walk. Later they discharged vermin regularly, especially after doses of vermifuge. Their faces gradually took on a certain stupid expression, their eyes became fixed and staring and their mouths were constantly drawn into a kind of smile. The upper and lower extremities were moving practically all the time,

though not violently, and their speech was growing inarticulate. But it was particularly from the seventh year that their condition constantly grew worse. Their fingers began to make painful contractions, and these painful movements gradually crept upwards into the hands and the forearms and upper arms. During the development of the disease the upper extremities at times had the following position: They were drawn backwards with hands almost touching behind and elbows turned outwards and forwards, quite stiff and immobile. Before these movements of the upper extremities had got above the elbows similar changes began to take place in the lower extremities: Painful movements turned the toes inwards and the heels apart. Then the legs were bent and finally the thighs, causing the heels to lie under the buttocks. This was the position of the dying girl. In the two deceased boys the position was said to have been not quite so marked. The parents had managed to straighten their legs, but they had immediately returned to their twisted position. It was impossible for the doctor to straighten out the lower extremities of the girl. To the parents it had seemed as if the children had no control of their muscles. They were of opinion that the children were intellectually normal. During the course of the disease their sight was impaired: It was difficult for them to see when the light was poor, but in daylight they seemed to see well. During the last phase of their lives a similar contraction of the muscles of the neck supervened, whereby the face was turned to one side and backwards, the chin resting on the shoulder. When the children died they were exceedingly lean.

Regarding the fourth child, the girl who was seven years old when examined, the district physician says: Pains and contractions of the whole of the upper extremities had already appeared but to a less degree and with remissions. There were movements of a few seconds' duration of the upper extremities: Her arms were bent are-like, causing the elbows to turn outwards and forwards, the backs of the hands almost touching the trochanteres majores. They regained a normal position. The patient seemed to lack control of the voluntary muscles. When a box was held up before her she reached for it several times before she managed to catch hold of it. The reason for this may have been that her eyesight was poor by lamp-light. She did not seem to look out when she walked; many bruises and wounds showed that she was always falling and hurting herself. This had also been the case with her deceased brothers and sisters.

A post mortem examination of the third child was made by the district physician, but the description is not sufficiently detailed. The cerebellum was found to be normal, likewise the liver.

The symptoms of the cases described by *P. Jensen* are those seen in heredofamilial progressive degenerations of the basal ganglions. There is no reason to suppose that vermin- or vermifuge have been of any significance. The symptomatology is extensive. There are features similar to those of cases described by *C. & O. Vogt*, *Spatz & Hallervorden*, *Kalinowsky*, and *Winkelman*. Thus we have before us a representative syndrome which may indicate a unity of these diseases. The comparatively rapid course of the disease may also indicate a particularly violent manifestation of a common basic disease.

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HISTOLOGICAL REPORT ON A CASE OF OLIGODENDROGLIOMA MALIGNUM IN THE CEREBRAL HEMISPHERE WITH METASTATIC EXTENSION TO THE CEREBELLUM

By

KNUD AAGE LORENTZEN

INTRODUCTION

In 1926 *Bailey* and *Cushing* (1) separated the oligodendrogliomas from the great group of cerebral gliomas. At that time it was difficult to make the oligodendroglia visible histologically by means of the silver methods. The authors were, however, able to demonstrate the special histological features that characterise these tumors (by means of the common staining methods), namely homogeneity of the cellular architecture, tendency to degeneration and calcification, few or no mitoses and a slow rate of growth. They concluded that the oligodendrogliomas were relatively benign tumors.

In 1929 *Bailey* and *Bucy* (2) gave a detailed description of the histology of the oligodendrogliomas. Their investigations were based upon 9 cases (of which only 4 were described in detail), and the silver methods were used on a large scale according to *Penfield* and *Globus*. It became obvious that the oligodendrocytes were neither so differentiated nor so uniform as first supposed. A great many of the tumor cells corresponded to the cells in the neural tube during the early stages of ontogeny. Cells representing transitional stages between oligodendrocytes were demonstrated, and in plenty. Mitoses were rare and metastatic spread was not shown within the central nervous system in any of the nine cases.

On reading through the above-mentioned article one begins to

suspect that the oligodendrogliomas may be more malignant than first believed.

In 1932 *Bailey* (3) wrote, too, that the oligodendrogliomas should always be treated with X-ray after operation because of their tendency to relapse.

In 1948 *Scheinker* (4) set up a special group of oligodendrogliomas: the malignant ones. He examined 8 such cases and found, besides the classical histological picture of the oligodendroglioma, pronounced multiformity of the cells and varying nuclear size, shape and amount of chromatin substance. Moreover mitoses were present and a great number of these were of an abnormal type. Finally the author called attention to the invasion of the cerebral cortex by the tumor cells and their accumulation within the pericellular spaces. In two cases metastatic nodules were found in the leptomeninges remote from the tumor itself, and in one case a regional metastasis in the vicinity of the main tumor.

Kwan and *Alpers* (5) described one case of oligodendroglioma with a small metastatic tumor in the leptomeninges remote from the main tumor.

In connection with the question of metastasis of multiplicity of the oligodendrogliomas within the central nervous system a case of malignant oligodendroglioma in the right cerebral hemisphere is presented below. At autopsy five years after operation a large oligodendroglioma was found in the central part of the left cerebellar hemisphere, besides a relapse of the main tumor in the right cerebral hemisphere.

CLINICAL REPORT

Married man (C.C.B.), 42 years old (b. 22.5.1906).

His father died of a brain tumor 42 years old.

No previous head injuries.

32 years old (1938) he got fits of right-sided headache and convulsions of the Jackson type in his left arm and leg. He was admitted to the Medical Department of the State Hospital, Sønderborg, on the 11th of November 1943 (case report 1863/43), when a decrease in the sense of sight and scintillating scotomas had developed. At the hospital a choked disc was found on both sides, and the liquor pressure was raised. Then he was transferred to the Neurosurgical Department of the University Hospital (Rigshospitalet), Copenhagen, (case report 4801). Ventriculography was performed and suspicion of a glioma on the dorsolateral border of the right parietal lobe arose. On operation such a glioma was found infiltrating the cerebral cortex. The tumor tissue had a greyish-red colour and contained a cyst as big as a walnut filled with a yellow fluid, which coagulated spontaneously. Cranially and caudally the tumor had broken through the wall of the lateral ventricle, which had to be opened, when the tumor was removed. After the operation he was treated with X-rays (3000 r).

Histological examination (Erna Christensen, M.D.) revealed an oligodendroglioma (malignum?).

For some time he got better (4 to 5 months), but then the Jackson fits recurred with increasing frequency, accompanied by an oppressing headache in the frontal region.

He was admitted to the Neurosurgical Department of the Municipal Hospital of Aarhus (case report 3780) on the 7th of July 1947. Here he was somewhat reduced mentally and had a left-sided spastic hemiparesis. Ophthalmoscopy revealed a faintly contoured disc on the left side. Ventriculography showed dilatation of the ventricle cavities and downward displacement of the right inferior horn. He was discharged again without treatment. Very soon he got worse, developing symptoms of vomitings in the morning, total blindness of the left eye, generalized convulsive attacks and disturbances of equilibrium. He was admitted again to the Medical Department of the State Hospital of Sønderborg (case report 1118/47) on the 11th of September 1947, but very soon discharged at the wish of his wife. During his stay at home his psychic symptoms grew worse, and on the 6th of December 1947 he was admitted to the State Mental Hospital of Augustenborg (case report 3686), where he died on the 22nd of May 1948.

BRAIN AUTOPSY

Gross appearance:

In the *right hemisphere* there is a very large defect on the dorsolateral surface extending from the upper part of the precentral gyrus to the parieto-occipital fissure. The parietal lobe is completely destroyed (fig. 1). The defect is partly filled with neoplastic tissue, which infiltrates the margins and the bottom and has broken through to the lateral ventricle. The tumor tissue has a greyish-red colour and numerous small hemorrhages are found.

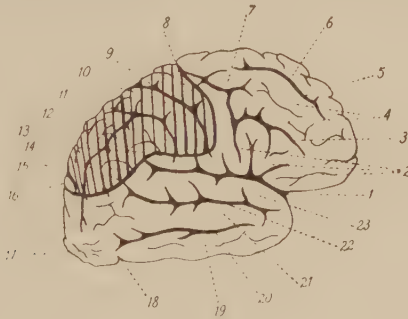


Fig. 1.

Extension of the cerebral tumor at autopsy.

A frontal section through the hemisphere shows the big tumor to have destroyed most of the white substance in the parietal lobe. Caudally it has extended to the upper part of the basal ganglia and surrounds the central part of the lateral ventricle. The brain tissue is very edematous. A *horizontal cut through the pons and the cerebellum* reveals a grey firm tumor in the central white of the left

cerebellar hemisphere (fig. 2). The tumor measures 4×4 cm. The vermis has been pushed to the right and the left dentate nucleus has been almost entirely destroyed. The tumor extends to the roof of the fourth ventricle, the cavity of which has been deformed. Small hemorrhages are visible in the tumor. No connection between the cerebral and cerebellar tumors was seen.

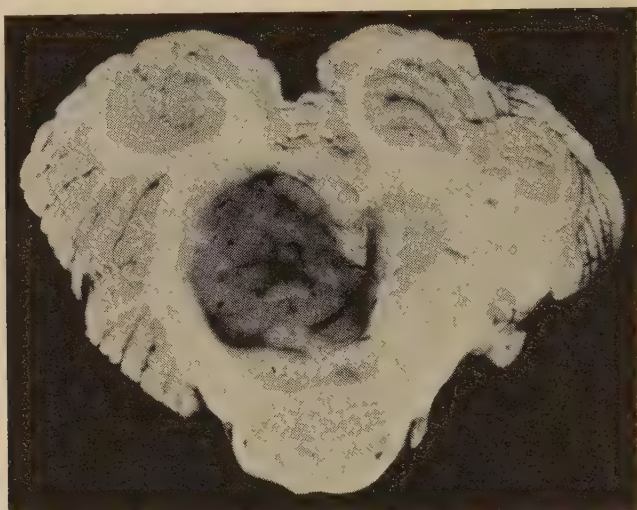


Fig. 2.
Metastatic tumor of the cerebellum.

Histological examination:

Tumor of the cerebral hemisphere (fig. 3), (hematoxylin-eosin and toluidin blue stain, *low magnification*): The picture is that of a typical oligodendroglioma: pronounced cellularity, rounded nuclei with medium chromatin content and each nucleus surrounded by a clear border of cytoplasm. The cells are arranged in small nests separated from each other by fine fibrillar septa. Moreover there are plenty of vessels, most of which are capillaries and small veins with thin walls. The vessels often form small conglomerates and convolutes. The perivascular connective tissue is increased, and there is a considerable accumulation of hyaline substances. In these areas the typical arrangement of the tumor cells is lacking, and the cells are degenerated, having pyknotic nuclei and scanty cytoplasm. There are in fact foci of necrosis and in close relation to these recent hemorrhages or accumulation of old blood pigment.

Calcium concrement formation is only scant.

Tumor of the cerebral hemisphere (fig. 4), (hematoxylin-eosin and toluidin blue stain, *high magnification*). Striking multiformity of the tumor cells is seen. Some nuclei are large and vesicular while others are small just as the nuclei of the typical oligodendrocytes. The shape of the nuclei also varies, and pronounced irregularity is not rare. Both typical and atypical mitoses are present, but they are not very numerous. The amount of cytoplasm varies much. Most frequently the large nuclei are surrounded by a broad border of cytoplasm without definite boundary. The cytoplasm is often granulated and sometimes vacuolated.

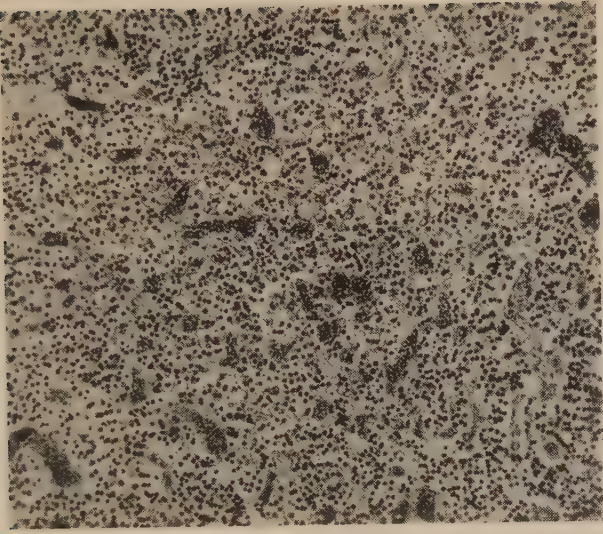


Fig. 3.
Cerebral tumor (low magnification).

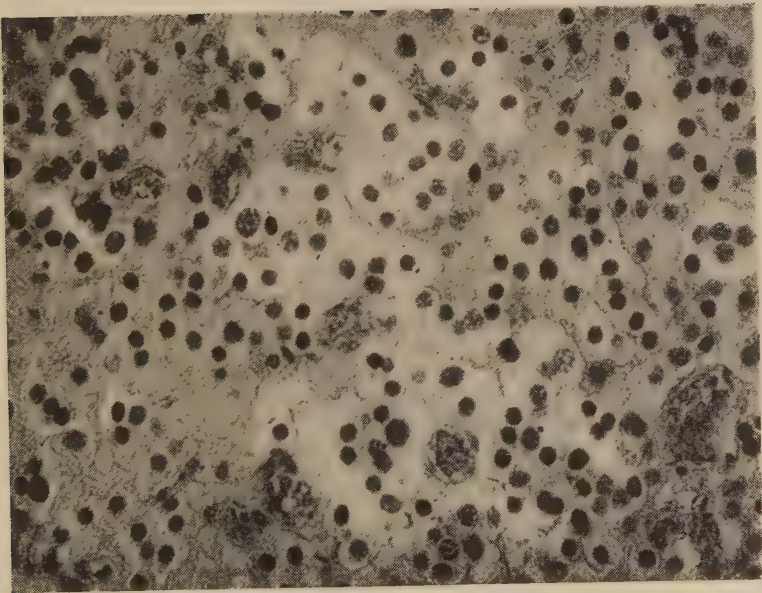


Fig. 4.
Cerebral tumor (high magnification).

In the degenerated areas the cytoplasm is homogeneous and has a slightly metachromatic hue and the cell boundaries are only poorly visible. The walls of the vessels show hyaline degeneration. The adventitia has proliferated, and new-formation of capillaries is seen.

Staining with Scharlach-rot reveals small droplets of fat in the vicinity of the hemorrhages.

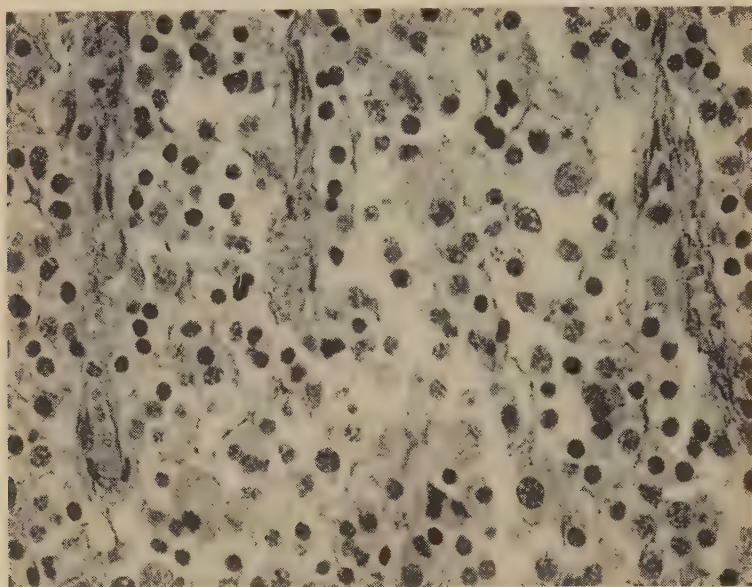


Fig. 5.
Cerebellar tumor (high magnification).

Preparations from the transitional zone between the cerebral tumor and the "normal tissue" show that the boundary of the tumor is not sharp. Moving away from the margin of the tumor the amount of neoplastic cells is seen to decrease gradually. When the cortical architecture is again clearly visible, the nerve cells are seen to be surrounded by numerous "satellites" consisting of typical oligodendrocytes and large tumor cells. Besides the pericellular accumulation of the tumor cells around the cell bodies of the nerve cells, collections of neoplastic cells are found along the dendrites and the axons and within the perivascular spaces. By these pericellular, intercellular, and perivascular pathways the neoplastic tissue has reached the subarachnoidal space where a regional metastasis is seen just on the superficial side of the main tumor.

In the white substance the interfascicular oligodendroglia is increased and in the vicinity of the main tumor a marked hyperplasia and hypertrophy of the astrocytes are found.

Tumor of the cerebellar hemisphere (fig. 5).

The histological appearance is mainly the same as that of the cerebral tumor. The large tumor cells are somewhat dominant and there are fewer hemorrhages and necroses.

Deposits of calcium are rare.

Preparations of the right corp. striatum, the thalamus, the subthalamie area, and the mesencephalon show that fine columns of the neoplastic tissue extend caudally via the external capsule, behind the posterior part of the lentiform nucleus into the sublenticular part of the internal capsule, reaching the most rostral part of the mesencephalon. From this area no connections to the cerebellar tumor are seen.

Preparations of the cerebral and cerebellar tumor treated with the silver methods of Penfield and Globus have been impregnated without success. Probably the tissue has been fixed too long in formalin.

Oligodendrocytes, varying considerably in size, can, however, be identified. Their processes are few and coarse.

Very large astrocytes and transitional cells are found together with a few spongioblasts.

COMMENT

The oligodendrogliomas represent only a small group of the intracranial tumors.

Cushing (6) found 27 among 2,023 intracranial tumors (1.3 %). In this material there were 862 gliomas so that the percentage of oligodendrogliomas within the glioma group was 3.1.

Courville (7) found only 3 oligodendrogliomas of 269 gliomas (1.1 %).

Löwenberg and Waggoner (9) found 21 oligodendrogliomas among 420 gliomas (5 %) and state that these tumors are not rare.

Apart from the aforementioned cases of oligodendrogliomas with metastatic extension to the leptomeninges and regional metastasis (*Scheinker, Kwan and Alpers*) only one case of metastatic extension from an oligodendroglioma has been reported by *Löwenberg and Waggoner* (9) (case 11). In this case the metastatic extension had taken place from one cerebral hemisphere to the other via the corpus callosum, and the connection between the two tumors was found to consist of collections of tumor cells within the perivascular spaces.

A similar mode of extension was observed by *Einarson and Neel* (8) in a case of diffuse glioblastoma and designated as "the type of indirect or metastatic extension" in contrast to "the type of direct or continuous extension" in which one could see the neoplastic tissue invading the brain parenchyma in continuity with the main tumor itself, but extending far away from it.

The question of metastatic extension of the gliomas within the brain itself has been discussed for many years, particularly in connection with multiple gliomas. In the main the debate on that problem has dealt with two possibilities: (1) Is there *only one primary tumor*,

which has extended metastatically within the brain itself just as primary maglinant tumors in other organs of the body extend metastatically within the organ itself or to other organs remote from the primary focus, or (2) Are there several *primary centres of neoplastic growth*, which develop at the same time or perhaps one after another? In connection with this *Courville* (7) examined 492 cases of intracranial tumors and found 21 cases (4.3 %) of multiple gliomas. Histologically these were distributed in the following manner: glioblastoma multiforme 14, astrocytoma 3, mixed types (glioblastoma multiforme + astrocytoma) 2, and atypical and transitional 2. He did not find any case of multiple oligodendroglioma, nor could any be found in the literature.

Moreover *Courville* has collected 113 cases of multiple intracranial tumors from the literature to find out their localization. He was able to find only four cases of cerebral and cerebellar glioma in the same brain.

It must be said therefore that the present case is unique as to the type of glioma and very rare as to the localization of the two tumors. In what way, however, shall we consider the origin of the cerebellar tumor?

Is it a metastatic extension (1) via the cerebral blood vessels, (2) via the perivascular spaces, as described by *Löwenberg* and *Wagoner* and *Einarson* and *Neel*, (3) via the ventricular cavities, or *is the tumor a direct continuation of the primary tumor* in the right cerebral hemisphere and consequently not a true metastasis in the common meaning of the word? *At last we must ask if the two tumors should be considered as originating from two separate primary centres of growth.*

Metastatic extension via the cerebral blood vessels can be excluded because of the anatomy of these vessels.

Metastatic extension via the perivascular spaces must be excluded, too, because this type of extension was not found microscopically. Indeed, collections of tumor cells in the perivascular spaces were seen, but only in the vicinity of the main tumor. Following the continuous growth downwards into the brain stem no accumulation of tumor cells within the perivascular spaces was seen.

Metastatic extension via the ventricle cavities cannot be entirely excluded. The tumor in the right cerebral hemisphere has broken through the wall of the lateral ventricle and on examining the cerebellar tumor the ependyma of the fourth ventricle is seen to be missing in several places, though this could be seen only under the microscope. Of course this may indicate that the cerebellar tumor has broken

through secondarily, and finally it may indicate that the ependyma has been lost during the preparation of the histological slices.

Courville says that even if the gliomas extend into the ventricle cavities, it has never been shown that the neoplastic tissue has invaded the brain substance from here. In a few cases collections of tumor cells have been observed in the third and fourth ventricle with the naked eye, but never invading the brain substance through the ependyma. *The present case shows however, that it is erroneous to dismiss the metastatic extension from a primary cerebral tumor to the brain substance via the ventricle cavities.* It seems rather possible that the focus of origin of the metastatic tumor may be of microscope size and consequently demonstrated only by using a very careful histological technique in the suspected area.

At an examination of the brain tissue between the cerebral and the cerebellar tumor the neoplastic tissue was followed via the capsula externa, behind the posterior part of the nucleus lentiformis, through the sublenticular part of the capsula interna to the cranial part of the mesencephalon. However, no connection from the mesencephalon to the cerebellar tumor was observed.

The extension of the neoplastic tissue into the brain stem was not visible with the naked eye, but under the microscope it was visible as slender columns of tumor cells making their way among the myelinated fibres (interneuronal extension) and inside the myelin sheaths along the axons (perineuronal extension).

As mentioned above, *Einarson and Neel* described this type of extension as direct or continuous in contrast to the indirect or metastatic within the perivascular spaces.

The present case, however, seems to show that a metastatic extension of gliomatous tissue may progress among the myelinated fibres and along the axons far away from the primary focus. Grossly the brain tissue between the main tumor and the metastasis was normal, but microscopically fine columns of tumor cells were seen to form the connection between the two tumors, apart from the short distance between the mesencephalon and the cerebellar tumor (see below). The brain tissue surrounding these fine columns of neoplastic tissue was well preserved. The present case, therefore makes it permissible to speak of metastatic or indirect extension of the neoplastic tissue even if there is no progression within the perivascular spaces to be seen.

The complete continuity from the main tumor to the cerebellar tumor was not seen, but in fact this is not necessary to regard the cerebellar tumor as a metastasis. *It seems plausible that the "vanguard*

cells" of the fine columns of the neoplastic tissue may work loose from the large tumor mass and by independent wandering within the inter- and perineuronal spaces reach a more remote place and start growing there as a metastasis.

The present case cannot definitely prove that a malignant oligodendroglioma can metastasize within the central nervous system by way of the inter- and perineuronal spaces, but it makes such a type of metastatical extension probable.

Courville in his work on the multiple gliomas concludes that these tumors always start growing in numerous primary, i.e. independent, centres. Certainly this is true in many cases, perhaps most of them, but not in all.

In the present case one might say, too, that the cerebellar tumor is independent, but this is only a postulate without basis in the actual facts.

SUMMARY

A 32 years old married man in 5 years gradually develops symptoms of an intracranial tumor. Operation reveals a malignant oligodendroglioma in the right parietal lobe near the dorsolateral border. The patient dies 5 years later (42 years old), and autopsy shows a relapse of the tumor in the right parietal lobe and, besides, a big tumor in the central white of the left cerebellar hemisphere. Histological examination shows that both tumors are oligodendrogliomas. The question of malignant gliomas metastasizing within the cerebrum is discussed.

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THE COPPER CONTENT IN CEREBROSPINAL FLUID IN ADULTS (AND CHILDREN) WITH AND WITHOUT SUFFERINGS IN THE CENTRAL NERVOUS SYSTEM

By

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The copper content of the cerebrospinal (cbs.) fluid has been made the object of rather few investigations.

Tompsett (7) by investigation of 4 samples of cbs. fluid obtained values between 32 and 67 γ %. He does not give any information whether these samples came from normal or sick persons. Considering that *Tompsett* finds twice as much copper in whole blood as other investigators his results must be treated with some scepticism. Other workers as a rule have found a lower copper content in cbs. fluid. *Yosikawa* (8) in 4 samples of "normal" cbs. fluid from uncomplicated cases of dementia praecox thus finds 14 to 15 γ % copper. *Axtrup* (1) has examined the copper content in cbs. fluid from 33 children (13 boys and 20 girls) aged 5 months to 10 years, his object being to study the cbs. fluid in cases with and without cerebral and meningeal affections. *Axtrup's* material consisted of 3 groups of almost equal size. The first group comprised children with different non-infectious diseases such as epilepsy and migraine. The second group contained children with infectious diseases like pharyngitis, pyuria, and endocarditis. The third group consisted of children with encephalitis, polyomyelitis, meningitis after parotitis, and tuberculous meningitis. In this last group there was generally increase in protein and cells. *Axtrup* found no differences between the copper content in the cbs. fluid in the 3 groups, the averages and limits (1 to 26 γ %) being almost the same.

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The present author has been of the opinion that it would also be of interest to publish an extensive examination of the copper content in the cbs. fluid in adults, both in "normal persons" and in patients with different diseases in the central nervous system and meninges.

METHODS

For the determination of copper in the cbs. fluid the same method was used as for serum copper. On the procedure of making use of the coloured compound formed by copper with sodium diethyldithiocarbamate, cf. a previous paper (5). Owing to the slight copper content of the cbs. fluid it is of the greatest importance that the lumbar syringes used for drawing the samples do not give off any copper. For that reason stainless V2A syringes were employed. That the syringes and stilettes were really copper-free was ascertained by rinsing them with redistilled water; the water used was analyzed and found to be copper-free. As a further precaution the first drops of cbs. fluid were not collected. In order to determine the copper content more accurately 2 ml. cbs. fluid for the single determination were used (instead of 1 ml. serum), and the analyses were performed in duplicate as usual. When a fixed amount of copper sulphate, weighed out and dissolved in redistilled water, is added to cbs. fluid with known copper content, the amount is recovered with an inaccuracy of a few per cent. By performing 10 analyses on the same cbs. fluid it was further demonstrated that copper can be recovered in this fluid with the same accuracy as in serum, i.e. the difference between the highest and lowest values not exceeding 10 γ %. Converted into 1 ml. sample this corresponds to a maximum deviation of 5 γ % in a duplicate determination. Occasionally the copper concentration of the cbs. fluid is lower than the maximum error, which involves a factor of uncertainty in the determination.

The cells in the cbs. fluid were counted in a Fuchs-Rosenthal counting-chamber. As a measure of the protein content in the cbs. fluid *Bisgaard's* (2) albumin and globulin numbers were used. From an investigation by *Ingerslev* (4) it appears that there is only a certain relationship between *Bisgaard's* albumin number and total protein when the latter is determined quantitatively by micro-Kjeldahl analyses (1 unit in albumin number corresponding to 1 to 4 mg % protein), the correlation not being closer until the protein content exceeds 60 mg %. The limits of normal findings in the cbs. fluid are put at a maximum of 15 for the albumin number and 1 for the globulin number, together with 10/3 per mm³ for cells.

CASE MATERIAL

The case material was obtained from the Neurological Department, Århus Municipal Hospital, a few patients, however, originating from the State Mental Hospital of Århus¹.

The material consisted of 62 men, 96 women, 11 boys, and 15 girls below 16 years. In 11 men and 2 women the cbs. fluid was examined twice and in 2 men and 1 woman three times. The material was divided into 3 groups. The first group consisted of patients with diseases which were found to be psychically conditioned, the diagnoses being neuroses, hysteria, psychopathy, and depression. The cbs. fluid in these persons showed normal content of protein and cells. This group of persons has been used as normal material, as it has not been possible to obtain cbs. fluid from quite healthy persons who might serve as basis of comparison with cbs. fluids which were significantly altered pathologically. The second group included patients with organic nervous diseases, but without changes in the cbs. fluid. The third group consisted of patients with pathologically altered cbs. fluids.

Further 3 experiments are presented with intravenous copper ingestion performed on the author with a view to the transference of copper from serum to cbs. fluid under normal conditions.

TABLE 1

Cerebrospinal Fluid Copper in Patients from a Neurological Department.

(C: Cells per mm³. A: Albumin number according to Bisgaard. G: Globulin number according to Bisgaard. K: Kahn's reaction for syphilis. M: Meinicke's reaction for syphilis. W: Wassermann's reaction for syphilis.—S.M.H.: State Mental Hospital of Århus).

Group 1

No.	Case	Sex & age	Diagnosis & remarks	Cbs. fluid copper in γ %	Other findings in the cbs. fluid
1	7605	♂ 30	Neurosis	15	C: 4/3, A: 14, G: 1, W: —
2	7150	♂ 27	Constitutional psychopathy	20	C: 3/3, A: 13, G: 1, W: —
	S.M.H.				
3	18849	♂ 41	"	13	C: 4/3, A: 8, G: 0, W: —
	S.M.H.				
4	19135	♂ 38	"	17	C: 6/3, A: 8, G: 0, W: —

¹ For the permission to use the last mentioned patients I am indebted to the Chief Physician: Erik Strömberg, M.D., Professor of Psychiatry.

No.	Case	Sex & age	Diagnosis & remarks	Cbs. fluid copper in %	Other findings in the cbs. fluid
	S.M.H.				
5	18734	♂ 36	Constitutional psychopathy	6	C: 4/3, A: 12, G: 0, W: —
6	7616	♀ 18	Neurosis	15	C: 2/3, A: 8, G: 1, W: —
7	6674	♀ 31	„	15	C: 0/3, A: 7, G: 1, W: —
8	7414	♀ 17	„	9	C: 1/3, A: 11, G: 1, W: —
9	7434	♀ 29	„	20	C: 0/3, A: 7, G: 1, W: —
10	6594	♀ 34	„	17	C: 2/3, A: 9, G: 1, W: —
11	7190	♂ 37	Depression	13	C: 3/3, A: 10, G: 1, W: —
12	„	♂ 37	„	11	C: 5/3, A: 8, G: 1, W: —
13	7652	♀ 31	Hysteria	8	C: 5/3, A: 7, G: 0, W: —
14	6547	♀ 21	„	7	C: 0/3, A: 6, G: 0, W: —
15	6735	♀ 8	Oligophrenia	9	C: 1/3, A: 7, G: 0, W: —
16	7289	♀ 10	Word-blindness	15	C: 4/3, A: 13, G: 1, W: —
<i>Group 2</i>					
17	6561	♀ 25	Neurosis + traumatic cephalalgia	12	C: 1/3, A: 10, G: 1, W: —
18	6560	♀ 22	Neurosis + cephalal- gia + nocturnal enu- resis	6	C: 4/3, A: 12, G: 0, W: —
19	6511	♀ 38	Neurosis + migraine	5	C: 0/3, A: 8, G: 0, W: —
20	6665	♀ 17	Neurosis + optic pseudoneuritis	10	C: 0/3, A: 10, G: 1, W: —
21	6410	♀ 24	Neurosis + graviditas	9	C: 0/3, A: 11, G: 1, W: —
22	7597	♀ 33	Neurosis + bronchial asthma	20	C: 3/3, A: 11, G: 1, W: —
23	6607	♀ 32	Neurotic cephalalgia	11	C: 3/3, A: 10, G: 1, W: —
24	6736	♀ 30	„	20	C: 2/3, A: 14, G: 1, W: —
25	6749	♀ 30	„	16	C: 1/3, A: 10, G: 1, W: —
26	7121	♂ 32	Migraine	11	C: 5/3, A: 12, G: 1, W: —
27	6420	♀ 24	„	18	C: 2/3, A: 8, G: 1, W: —

No.	Case	Sex & age	Diagnosis & remarks	Cbs. fluid copper in γ %	Other findings in the cbs. fluid
28	6436	♀ 30	Migraine	15	C: 5/3, A: 13, G: 1, W: —
29	6461	♀ 33	„	13	C: 1/3, A: 12, G: 1, W: —
30	6429	♀ 48	„	10	C: 4/3, A: 14, G: 1, W: —
31	6996	♂ 10	„	24	C: 1/3, A: 10, G: 1, W: —
32	7146	♂ 11	„	7	C: 0/3, A: 12, G: 1, W: —
33	6621	♀ 12	„	3	C: 2/3, A: 12, G: 1, W: —
34	7070	♀ 13	„	7	C: 1/3, A: 8, G: 1, W: —
35	7373	♀ 11	„	8	C: 1/3, A: 8, G: 1, W: —
36	6404	♀ 15	„	14	C: 2/3, A: 7, G: 0, W: —
37	7437	♂ 22	Cryptogenetic epilepsy	5	C: 2/3, A: 6, G: 0, W: —
38	7296	♂ 25	„	18	C: 7/3, A: 11, G: 1, W: —
39	7572	♂ 21	„	9	C: 3/3, A: 10, G: 1, W: —
40	6387	♀ 43	„	9	C: 2/3, A: 6, G: 0, W: —
41	7239	♀ 18	„	14	C: 1/3, A: 13, G: 1, W: —
42	6634	♂ 1	„	5	C: 0/3, A: 12, G: 1, W: —
43	7273	♂ 10	„	14	C: 8/3, A: 6, G: 0, W: —
44	6489	♂ 1	Symptomatic epilepsy- atrophic cerebral affection	6	C: 1/3, A: 6, G: 0, W: —
45	6658	♀ 6	Cryptogenetic epilepsy	8	C: 4/3, A: 5, G: 0, W: —
46	7384	♀ 16	„	11	C: 4/3, A: 7, G: 0, W: —
47	7447	♀ 9	„	17	C: 1/3, A: 7, G: 1, W: —
48	7293	♀ 3	Symptomatic epilepsy + microcephalia + idiotism	12	C: 0/3, A: 10, G: 1, W: —
49	6942	♀ 11	Traumatic epilepsy	16	C: 3/3, A: 8, G: 0, W: —
50	6380	♀ 52	Chromophobe adenoma (before operation)	25	C: 1/3, A: 14, G: 1, W: —
51	6551	♀ 26	Chronic epidemic encephalitis	12	C: 1/3, A: 9, G: 1, W: —

No.	Case	Sex & age	Diagnosis & remarks	Cbs. fluid copper in γ %	Other findings in the cbs. fluid
52	7607	♀ 10	Subthalamic encephalitis	13	C: 8/3, A: 5, G: 0, W: —
53	6579	♀ 42	Multiple sclerosis	13	C: 3/3, A: 12, G: 1, W: —
54	6464	♀ 37	„	3	C: 0/3, A: 9, G: 1, W: —
55	6742	♀ 47	Intraspinal disc prolapse	13	C: 0/3, A: 12, G: 1, W: —
56	6728	♀ 56	Infectious myelitis	20	C: 2/3, A: 12, G: 0, W: —
57	6599	♀ 52	Chronic polyneuritis	8	C: 3/3, A: 10, G: 1, W: —
58	6537	♀ 53	Cbs. syphilis-incipient tabes dorsalis	8	C: 5/3, A: 8, G: 0, W: — W. in blood: dubious
59	6827	♀ 56	„ before treatment	6	C: 1/3, A: 12, G: 1, W: $\pm$ W. in blood: 7, K: 4, M: weak: +
„	„	„ „	New sample before treatment	12	C: 5/3, A: 12, G: 1, W: $\pm$
60	6887	♀ 40	Cbs. syphilis-incipient dementia paralytica (after treatment with penicillin and hyper- therm)	14	C: 4/3, A: 12, G: 1, W: — W. in blood: 4, K: 3, M: weak: $\pm$
61	7053	♀ 32	Cbs. syphilis-tabes dorsalis	17	C: 2/3, A: 10, G: 1, W: — W. in blood: —
62	7089	♀ 32	Syphilis of unknown origin	12	C: 4/3, A: 6, G: 0, W: — W. in blood: 8, K: 9, M: strong: +
63	7163	♀ 53	Cbs. syphilis-incipient tabes dorsalis-demen- tia paralytica-syphili- tic neurolabyrinthitis	16	C: 2/3, A: 11, G: 1, W: — W. in blood: —, K: 4, M: strong: +
64	7021	♀ 34	Chronic syphilitic me- ningitis—cbs. syphilis- sanative tabes dorsalis	11	C: 1/3, A: 8, G: 1, W: — W. in blood: 1, K: —, M: dubious: $\pm$
65	7285	♂ 68	Amyotrophic lateral sclerosis	10	C: 0/3, A: 10, G: 1, W: —

No.	Case	Sex & age	Diagnosis & remarks	Cbs. fluid copper in γ %	Other findings in the cbs. fluid
66	6519	♀ 28	Spastic torticollis- degeneration of corpus striatum	8	C: 6/3, A: 12, G: 1, W: —
67	6559	♀ 24	Little's disease	14	C: 2/3, A: 10, G: 0, W: —
68	6358	♀ 2	„	10	C: 2/3, A: 6, G: 0, W: —
69	6696	♀ 49	Progressive bulbar paralysis	8	C: 0/3, A: 9, G: 0, W: —
70	6781	♀ 45	Gastrogenic myelosis	5	C: —, A: 12, G: 1, W: —
71	7588	♀ 37	Myxoedema + depres- sion	21	C: 3/3, A: 8, G: 0, W: —
72	6385	♀ 10	Neurolabyrinthitis	8	C: 3/3, A: 15, G: 1, W: —
73	6391	♀ 15	Stenosis of aqueduct of Sylvius	7	C: 0/3, A: 6, G: 0, W: —
<i>Group 3</i>					
74	7537	♂ 40	Neurosis + cephalal- gia	12	C: 5/3, A: 14, G: 1-2, W: —
75	7346	♂ 25	Neurosis + nocturnal enuresis	17	C: 2/3, A: 12, G: 1-2, W: —
76	7197	♂ 15	„	10	C: 17/3, A: 12, G: 1, W: —
77	6482	♀ 23	Neurosis + oligo- phrenia	10	C: 4/3, A: 16, G: 2, W: —
78	6510	♀ 39	Neurosis	4	C: 4/3, A: 14, G: 1-2, W: —
79	6550	♀ 19	Neurosis + traumatic cephalgia	7	C: 12/3, A: 9, G: 1, W: —
80	6424	♀ 41	„	9	C: 4/3, A: 15, G: 1-2, W: —
81	7409	♀ 17	Neurosis + hyper- ventilation tetany	14	C: 6/3, A: 17, G: 1-2, W: —
82	6369	♀ 22	Neurosis + hypometab- olism + cephalgia	14	C: 3/3, A: 17, G: 2, W: —
83	6753	♀ 21	Neurosis + cephalal- gia + arachnoiditis	7	C: 5/3, A: 16, G: 1, W: —
84	7242	♂ 57	Neurotic cephalgia	15	C: 6/3, A: 15, G: 1-2, W: —
85	6448	♀ 21	„	6	C: 2/3, A: 17, G: 2, W: —

No.	Case	Sex & age	Diagnosis & remarks	Cbs. fluid copper in γ %	Other findings in the cbs. fluid
86	7269	♀ 40	Neurotic cephalalgia + incipient climac- terium	22	C: 1/3, A: 15, G: 1-2, W: —
87	6517	♀ 19	Cryptogenetic cephal- algia	8	C: 4/3, A: 14, G: 1-2, W: —
88	6625	♀ 25	„	23	C: 2/3, A: 18, G: 2, W: —
89	6416	♀ 34	Migraine + adipositas	5	C: 7/3, A: 16, G: 1-2, W: —
90	6476	♀ 60	Migraine	15	C: 5/3, A: 16, G: 2, W: —
91	6457	♀ 41	Depression	2	C: 11/3, A: 9, G: 1, W: —
92	6400	♀ 30	Hysteria	9	C: 0/3, A: 16, G: 1-2, W: —
93	7492	♂ 34	Cryptogenetic epilepsy	23	C: 3/3, A: 20, G: 2, W: —
94	7479	♂ 18	„	10	C: 3/3, A: 21, G: 1-2, W: —
95	7286	♂ 25	„	7	C: 21/3, A: 15, G: 1-2, W: —
96	7514	♂ 20	„	5	C: 2/3, A: 22, G: 2, W: —
97	6376	♂ 1	„	13	C: 6/3, A: 17, G: 2, W: —
98	6522	♀ 9	„	9	C: 14/3, A: 12, G: 1, W: —
99	7620	♂ 5	Symptomatic epilepsy	10	C: 17/3, A: 18, G: 2, W: —
100	7273	♂ 36	Cystic frontotemporal glioma (before opera- tion)	14	C: 13/3, A: 26, G: 2-3, W: —
101	6515	♀ 53	Frontal glioma (be- fore operation)	4	C: 0/3, A: 16, G: 1-2, W: —
102	7553	♀ 24	Parasagittal meninge- oma (before opera- tion)	8	C: 6/3, A: 15, G: 1-2, W: —
103	7326	♂ 58	Chronic epidemic encephalitis	9	C: 3/3, A: 19, G: 1-2, W: —
104	7494	♂ 25	„	3	C: 3/3, A: 16, G: 1-2, W: —
105	7584	♂ 50	Parkinsonism	10	C: 3/3, A: 14, G: 1-2, W: —
106	6460	♀ 57	Chronic epidemic encephalitis	17	C: 1/3, A: 16, G: 1-2, W: —
107	6368	♀ 51	„	8	C: 3/3, A: 24, G: 2-3, W: —

No.	Case	Sex & age	Diagnosis & remarks	Cbs. fluid copper in γ %	Other findings in the cbs. fluid
108	6447	♀ 46	Chronic epidemic encephalitis	18	C: 3/3, A: 24, G: 2, W: —
109	7177	♀ 38	Encephalitis of mes- encephalon	13	C: 23/3, A: 29, G: 2, W: —
110	7320	♀ 44	Paralysis agitans	15	C: 2/3, A: 21, G: 2, W: —
111	6396	♀ 65	„	12	C: 2/3, A: 14, G: 1-2, W: —
112	7582	♂ 67	Cbs. arteriosclerosis + inferior spastic para- paresis	8	C: 3/3, A: 21, G: 2, W: —
113	6938	♂ 58	Cerebral arterio- sclerosis	12	C: 2/3, A: 17, G: 2, W: —
114	7542	♂ 65	Cerebral arteriosclero- sis + Parkinsonism	8	C: 0/3, A: 18, G: 1-2, W: —
115	6405	♀ 62	Medullar arterio- sclerosis	9	C: 4/3, A: 14, G: 1-2, W: —
116	7508	♂ 48	Multiple sclerosis	23	C: 9/3, A: 21, G: 2, W: —
117	6320	♀ 32	„	10	C: 16/3, A: 16, G: 1-2, W: —
118	6423	♀ 29	„ before treatment	6	C: 6/3, A: 21, G: 2, W: —
„	„	„ „	Multiple sclerosis after treatment with ultraviolet radiation, arsenic and liver pre- paration	13	C: 6/3, A: 16, G: 2, W: —
119	6435	♀ 42	Multiple sclerosis	9	C: 6/3, A: 38, G: 4, W: —
120	6449	♀ 29	„	3	C: 7/3, A: 25, G: 3, W: —
121	6629	♀ 59	„	6	C: 8/3, A: 17, G: 2, W: —
122	6656	♀ 26	„	17	C: 9/3, A: 19, G: 2, W: —
123	6770	♀ 27	„	5	C: 23/3, A: 22, G: 2, W: —
124	6325	♀ 45	„	10	C: 12/3, A: 24, G: 2-3, W: —
125	7056	♀ 59	„	13	C: 0/3, A: 14, G: 1-2, W: —
126	6956	♂ 51	Syringomyelia	11	C: 2/3, A: 18, G: 2, W: —

No.	Case	Sex & age	Diagnosis & remarks	Cbs. fluid copper in γ %	Other findings in the cbs. fluid
127	7604	♂ 28	Syringomyelia	9	C: 2/3, A: 15, G: 1-2, W: —
128	7640	♂ 33	„	11	C: 1/3, A: 15, G: 1-2, W: —
129	7663	♂ 48	„	9	C: 0/3, A: 15, G: 1-2, W: —
130	7528	♂ 46	Muscular atrophy of neural origin + Parkinsonism	16	C: 5/3, A: 18, G: 2, W: —
131	7060	♂ 34	Myotonia atrophica	18	C: 0/3, A: 16, G: 1-2, W: —
132	6469	♀ 38	Intraspinal disc prolapse	3	C: 1/3, A: 18, G: 2, W: —
133	6533	♀ 21	„	11	C: 0/3, A: 16, G: 1-2, W: —
134	6425	♀ 64	Lumbosacral hemato- myelia	8	C: 22/3, A: 18, G: 2, W: —
135	7536	♂ 21	Myelitis after infection	17	C: 6/3, A: 19, G: 2, W: —
„	„	„ „	„ fresh outbreak, but af- ter penicillin for 3 days	9	C: 188/3, A: 140, G: 12, W: —
136	7132	♂ 55	Neuromyelitis optica	22	C: 0/3, A: 45, G: 5, W: —
137	7408	♀ 18	Acute encephalo- myelitis	6	C: 56/3, A: 18, G: 1-2, W: —
138	7248	♀ 32	Acute anterior polio- myelitis (paralytic form)	6	C: 8/3, A: 45, G: 4, W: —
139	6771	♀ 53	Acute anterior polio- myelitis	14	C: 604/3, A: 88, G: 9, W: —
140	7292	♂ 38	Cryptogenic subacute polyneuritis	7	C: 3/3, A: 25, G: 2-3, W: —
141	6500	♂ 40	Polyradiculoneuritis from porphyria	8	C: 0/3, A: 20, G: 2, W: —
142	7661	♀ 29	Basal cerebral arach- noiditis	9	C: 461/3, A: 54, G: 5, W: —
143	6250	♀ 22	Primary chronic lym- phocytic meningitis	7	C: 69/3, A: 24, G: 2, W: —
144	7617	♀ 28	Lymphocytic meningi- tis	19	C: 8576/3, A: 45, G: 4, W: —

No.	Case	Sex & age	Diagnosis & remarks	Cbs. fluid copper in %	Other findings in the cbs. fluid
145	6545	♂ 10	Tuberculous meningitis	6	C: 1072/3, A: 58, G: 5, W: —
146	6403	♂ 50	Cbs. syphilis	34	C: 2/3, A: 60, G: 5-6, W: — W. in blood: —
147	6619	♂ 50	„ before treatment	14	C: 198/3, A: 38, G: 3-4, W: 9, M: weak: +, W. in blood: 1, K: 4, M: weak: +
„	„	„ „	Cbs. syphilis after treatment with penicillin and hyper- therm	9	C: 129/3, A: 45, G: 6, W: 6, M: weak: +, W. in blood: 5, K: 6, M: weak: +
148	7003	♂ 55	Cbs. syphilis before treatment	19	C: 43/3, A: 50, G: 4-5, W: 4, M: dubious: + W. in blood: —
„	„	„ „	Cbs. syphilis after treatment with penicillin and hyper- therm	16	C: 13/3, A: 40, G: 3-4, W: 2, M: dubious: ± W. in blood: —
149	7208	♂ 29	Cbs. syphilis	7	C: 20/3, A: 31, G: 3, W: 13, M: weak: +, W. in blood: 4, K: 3, M: weak: +
150	7636	♂ 44	„ before treatment	7	C: 40/3, A: 38, G: 3, W: 5, M: strong: +, W. in blood: 10, K: 9, M: weak: +
„	„	„ „	Cbs. syphilis after treatment with penicillin	3	C: 40/3, A: 40, G: 3, W: 4, M: strong: +
151	6610	♂ 44	Cbs. syphilis	5	C: 12/3, A: 18, G: 2, W: — W. in blood: —
152	6585	♂ 22	Congenital cbs. syphi- lis-dementia paralytica before treatment	8	C: 4/3, A: 23, G: 2, W: 6, M: strong: +, W. in blood: 8, K: 2, M: dubious: ±
„	„	„ „	Congenital cbs. syphi- lis-dementia paralytica after treatment with penicillin	15	C: 7/3, A: 18, G: 2, W: 6, M: dubious: ±, W. in blood: 7, K: 5, M: dubious: ±
153	6520	♂ 38	Cbs. syphilis-dementia paralytica	6	C: 176/3, A: 60, G: 5, W: 3, M: strong: +, W. in blood: 7, K: 5, M: strong: +

No.	Case	Sex & age	Diagnosis & remarks	Cbs. fluid copper in %	Other findings in the cbs. fluid
154	6534	♂ 44	Cbs. syphilis-incipient dementia paralytica- endarteritis obliterans before treatment	7	C: 52/3, A: 55, G: 5, W: 10, M: strong: +, W. in blood: 11, K: 2, M: strong: +
"	"	" "	Cbs. syphilis-incipient dementia paralytica- endarteritis obliterans after treatment with penicillin	10	C: 21/3, A: 40, G: 3, W: 10, M: strong: +
"	"	" "	Cbs. syphilis-incipient dementia paralytica- endarteritis obliterans after treatment with hypertherm, salvarsan, and bismuth	7	C: 3/3, A: 26, G: 2-3, W: 13, M: strong: +, W. in blood: 9, K: 1, M: weak: +
155	6951	♂ 40	Cbs. syphilis-dementia paralytica before treatment	25	C: 35/3, A: 80, G: 8, W: 9, M: strong: +, W. in blood: 18, K: 10, M: strong: +
"	"	" "	Cbs. syphilis-dementia paralytica after treatment with penicillin, salvarsan, and bismuth	15	C: 68/3, A: 80, G: 7-8, W: 6, M: strong: +
	S.M.H.				
156	18853	♂ 39	Cbs. syphilis-dementia paralytica	19	C: 207/3, A: 20, G: 1, W: 9, M: strong: +, W. in blood: 5, K: 4, M: weak: +
	S.M.H.				
157	18861	♂ 40	"	6	C: 249/3, A: 40, G: 2, W: 5, M: strong: +, W. in blood: —, K: 2, M: dubious: ±
	S.M.H.				
158	15341	♂ 55	"	13	C: 19/3, A: 10, G: 0, W: 5, M: strong: +, W. in blood: 11, K: 9, M: strong: +
	S.M.H.				
159	18812	♂ 47	"	21	C: 13/3, A: 15, G: 1, W: 2, M: dubious: ±, W. in blood: 1, K: 3, M: weak: ±
160	6721	♂ 51	"	8	C: 7/3, A: 21, G: 2, W: —, W. in blood: —, K: —, M: dubious: ±

No.	Case	Sex & age	Diagnosis & remarks	Cbs. fluid copper in %	Other findings in the cbs. fluid
161	7040	♂ 63	Cbs. syphilis-incipient dementia paralytica	10	C: 6/3, A: 22, G: 2, W: —, M: dubious: $\pm$, W. in blood: 5, K: 5, M: strong: +
162	6421	♂ 48	Cbs. syphilis-tabes dorsalis before treatment	19	C: 172/3, A: 75, G: 8, W: 3, M: strong: +, W. in blood: 5, K: 8, M: strong: +
"	"	" "	Cbs. syphilis-tabes dorsalis after treatment with penicillin	4	C: 68/3, A: 45, G: 5, W: 2, M: strong: +
"	"	" "	Cbs. syphilis-tabes dorsalis after treatment with hypertherm, salvarsan, and bismuth	9	C: 22/3, A: 23, G: 2, W: 1, M: weak: +, W. in blood: 4, K: 10, M: strong: +
163	6760	♂ 43	Cbs. syphilis-incipient tabes dorsalis after treatment with penicillin and hyper- therm	10	C: 13/3, A: 15, G: 1, W: 4, M: strong: +, W. in blood: —, K: —, M: dubious: $\pm$
164	7235	♂ 74	Cbs. syphilis-tabes dorsalis before treatment	14	C: 605/3, A: 43, G: 4, W: 6, M: strong: +, W. in blood: 10, K: 11, M: strong: +
"	"	" "	Cbs. syphilis-tabes dorsalis after treatment with penicillin	10	C: 162/3, A: 38, G: 3-4, W: 5, M: strong: +, W. in blood: 10, K: 9, M: strong: +
165	7001	♂ 49	Cbs. syphilis-tabes dorsalis	11	C: 5/3, A: 20, G: 2, W: —, W. in blood: —, K: 1, M: dubious: $\pm$
166	7128	♂ 57	Cbs. syphilis-incipient tabes dorsalis and de- mentia paralytica before treatment	12	C: 292/3, A: 55, G: 5, W: 5, M: strong: +, W. in blood: 1, K: 2, M: dubious: $\pm$
"	"	" "	Cbs. syphilis-incipient tabes dorsalis and de- mentia paralytica after treatment with penicillin, hypertherm, salvarsan, and bis- muth	10	C: 139/3, A: 45, G: 4, W: 5, M: strong: +, W. in blood: 2, K: 1, M: dubious: $\pm$

No.	Case	Sex & age	Diagnosis & remarks	Cbs. fluid copper in γ %	Other findings in the cbs. fluid
167	6960	♂ 56	Cbs. syphilis-tabes dorsalis-incipient de- mentia paralytica before treatment	22	C: 5/3, A: 27, G: 2, W: 2, M: dubious: $\pm$, W. in blood: 1, K: 2, M: dubious: $\pm$
"	"	" "	Cbs. syphilis-tabes dorsalis-incipient de- mentia paralytica after treatment with penicillin	13	C: 7/3, A: 17, G: 1-2, W: 2, M: dubious: $\pm$, W. in blood: 2, K: 1, M: dubious: $\pm$
168	7004	♂ 44	Sanative cbs. syphilis- spinal arachnoiditis before treatment	10	C: 0/3, A: 20, G: 2, W: —, W. in blood: —
"	"	" "	Sanative cbs. syphilis- spinal arachnoiditis after treatment with hypertherm	14	C: 4/3, A: 19, G: 1-2, W: —
169	6712	♀ 62	Cbs. syphilis	10	C: 5/3, A: 57, G: 6, W: 7, M: strong: +, W. in blood: 6, K: 6, M: weak: +
170	7123	♀ 58	" before treatment	7	C: 25/3, A: 28, G: 3, W: —, W. in blood: 7, K: 9, M: strong: +
"	"	" "	Cbs. syphilis after treatment with penicillin	10	C: 25/3, A: 30, G: 3, W: —, W. in blood: 8, K: 10, M: strong: +
171	7181	♀ 64	Cbs. syphilis	19	C: 8/3, A: 15, G: 1-2, W: —, W. in blood: —
172	6249	♀ 64	Cbs. syphilis-incipient dementia paralytica after treatment with penicillin, hypertherm, salvarsan, and bismuth	9	C: 5/3, A: 25, G: 2, W: 6, M: strong: +, W. in blood: 1, K: 2, M: strong: +
S.M.H.					
173	19075	♀ 50	Cbs. syphilis-dementia paralytica	12	C: 14/3, A: 15, G: 1, W: 5, M: strong: +, W. in blood: not drawn
174	7007	♀ 58	Cbs. syphilis-incipient dementia paralytica	12	C: 9/3, A: 15, G: 1-2, W: 3, M: —: $\pm$, W. in blood: —, K: 2, M: weak: $\pm$

No.	Case	Sex & age	Diagnosis & remarks	Cbs. fluid copper in γ %	Other findings in the cbs. fluid
175	7178	♀ 37	Cbs. syphilis-incipient tabes dorsalis	11	C: 18/3, A: 26, G: 3, W: 1, M: dubious: $\pm$, W. in blood: 4, K: 4, M: dubious: +
59	6827	♀ 56	Cbs. syphilis-incipient tabes dorsalis after treatment with penicillin and hyper- therm	12	C: 4/3, A: 27, G: 2, W: 1, M: —: $\pm$, W. in blood: 7, K: 3, M: strong: +
176	6348	♀ 44	Cbs. syphilis-Sepsis	16	C: 13/3, A: 32, G: 3, W: 4, M: weak: +, W. in blood: 6, K: 7, M: strong: +
177	6967	♀ 35	Cbs. syphilis-syphilitic encephalomyelitis	9	C: 1/3, A: 20, G: 2, W: —, W. in blood: —
178	7266	♂ 57	Chronic alcoholism	19	C: 14/3, A: 25, G: 2-3, W: —
179	6417	♀ 52	Hypertensive encephalopathy	6	C: 1/3, A: 16, G: 2, W: —
180	6488	♀ 24	Hepatolenticular degeneration	7	C: 7/3, A: 17, G: 1-2, W: —
181	6636	♀ 38	Acroparesthesia + Adie's syndrome	14	C: 2/3, A: 6, G: 0, W: —
182	6748	♀ 25	Sturge's-Weber's- Dimitri's-Krabbe's disease	16	C: 0/3, A: 17, G: 1-2, W: —
183	7217	♀ 21	Lupus erythematosus disseminatus	9	C: 37/3, A: 42, G: 4, W: —
184	7585	♂ 15	Lipothymia-vasovagal fits	13	C: 1/3, A: 14, G: 1-2, W: —

RESULTS

All the results are listed in Table 1. In the three groups into which the table is divided, men, women, boys, and girls are entered separately, just as a division according to diagnosis was carried out. Age and number of the journal are stated. The results of the copper determinations and the other findings in the cbs. fluid are listed separately.

It appears from the results for group 1 in the table that the average and limits of the copper content in cbs. fluid are the same

for men and women, the average for 7 men being 13.57 γ % (range: 6 to 20) and for 7 women 13.00 γ % (range: 7 to 20). As the material in group 1 is small it is unjustifiable to attach too much importance to the limits found; the results for 2 girls aged 8 and 10 in group 1 are in good agreement with the values of copper in cbs. fluid found for adults. They are also consistent with the values found for children by Axtrup (see above).

Group 2 comprises patients with neurological diseases, but without changes in cbs. fluid. As a whole cbs. fluid copper is found to be within the same limits as in group 1, but both somewhat higher and lower copper values occur than in the first group. The average, 11.67 γ %, is thus a little lower than in group 1, the difference, however, not being significant ($t = 1.13$). The high values as well as the low ones appear in connection with different diseases.

In the third and largest group where there are positive findings in the cbs. fluid the majority of the values lie within the limits found for group 1, but a few values pass beyond them. The average, 11.31 γ %, again is a little lower than in group 2, but not significantly different from the mean value of group 1 ($t = 1.52$). Neither is the difference between the averages for group 2 and 3 significant ($t = 0.43$). Also in the third group the extreme values are found in patients with different diagnoses. It should be noted that the cbs. fluid copper is not raised in four cases of arachnoiditis and meningitis (Nos. 142 to 145) with enhanced cell values, in which case one would suppose the serum-liquor barrier to fail. In the cases of patients with syphilis in which cbs. fluid copper was examined before and after treatment with penicillin and hypertherm no certain basis was obtained for showing that the treatment has any influence on the copper concentration. It should be especially emphasized that on the basis of the material presented one cannot assume that there is any relationship between the contents of protein and copper in cbs. fluid. For this reason the author did not feel that there was any basis for extending the examinations for the purpose of a quantitative determination of the protein content in cbs. fluid.

It appears from Table 1 that there is no influence of sex, nor of age.

From the present material it is possible to state that the determination of copper in cbs. fluid cannot be supposed to have any diagnostic or prognostic importance.

The ratios of protein divided by copper in serum and in cbs. fluid do not correspond quantitatively. There is relatively much more copper in the cbs. fluid. This fact is not easily explained as all the copper in serum seems to be bound to protein, and copper added to serum cannot further be bound to protein (*Holmberg & Laurell* (3)).

The author made some experiments on himself concerning the transition of copper into the cbs. fluid. The procedure in these experiments was to put in a lumbar syringe à demeure for 2 hours and during this time to draw cbs. fluid at regular intervals for the copper determination, both in connection with intravenous copper ingestion and without. 3 experiments were carried out with intervals of a couple of months; in each experiment 5 samples of 5 ml. cbs. fluid were taken, i.e. immediately after the puncture, after 5 minutes, after 30 minutes, after 1 hour and after 2 hours respectively. In each experiment cell number, albumin- and globulin number were determined in the first sample, and normal conditions were found. The experiment in which no copper was administered served as control for the 2 others in which, after the drawing of the first sample of cbs. fluid, 10 cg. of Ebesal was given intravenously (Ebesal is a complex, water-soluble copper salt, sodium cuproallylthiourea benzozoate, which contains 19 % copper). In order to ascertain that there is really an increase in the copper content of serum after the intravenous copper administration, copper was also determined immediately before and 5 minutes after ingestion of Ebesal, and in both experiments a fourfold increase in serum copper was observed. In an experiment with intravenous administration of Ebesal it was shown that the copper concentration in serum reaches the normal value again in the course of 2 hours (6). The results are listed in Table 2.

TABLE 2
Cerebrospinal Fluid Copper after Intravenous Ingestion of Ebesal by Means of a Syringe à Demeure for 2 Hours

Cbs. fluid copper in γ %	1. Control experiment	2. Experiment with 10 cg. Ebesal	3. As in experiment 2
Initial value	18	19	11
After 5 minutes	11	9	15
After 30 minutes	6	8	9
After 60 minutes	5	9	8
After 120 minutes	12	11	12
Average of last 4 values	9	9	11

It appears from Table 2 that the values before copper charging show great variations. Similarly the four values after the intravenous copper administration are subject to irregular fluctuations. However,

the averages of the 4 values mentioned are almost identical in the three experiments, the mean being 9 γ % without administration of copper and 9 and 11 γ %, respectively, in the experiments with charging of Ebesal. The author is of opinion that there is no basis for assuming that copper passes from blood to cbs. fluid under a strong artificial increase in serum copper.

SUMMARY

The investigations on the copper concentration in cbs. fluid from patients with neurological and psychic sufferings show that the copper concentration of the cbs. fluid in the 3 groups examined is of the same order of magnitude. It is independent of sex and age. The copper content is not influenced by the protein concentration in the cbs. fluid, nor by affections in the meninges. A transition of copper from blood to cbs. fluid does not occur under a sudden artificial increase in serum copper caused by intravenous administration of copper.

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DETERMINATIONS OF GLUTAMINE AND GLUTAMIC ACID IN A MATERIAL OF MENTAL PATIENTS

Preliminary Report¹

By

IB MUNKVAD

As part of the research scheme within the field of biochemistry of the Department for Men in the Sankt Hans Mental Hospital about 150 determinations of glutamine and glutamic acid in patients with mental affections have been carried within the last six months.

Glutamic acid, according to *Weil-Malherbe* (26), is the only amino acid which is converted in the cerebrum; moreover, this acid is of vital importance in the aminating, desaminating, and transaminating processes (5, 6, 7, 12). The importance of glutamic acid and glutamine in the formation of urea in the liver and ammonia in the kidney, respectively, has been demonstrated by a number of previous authors (2, 4, 24). According to *Nachmansohn* (18), glutamic acid acts as a coenzyme in the formation of choline acetylase, thereby influencing the production of acetylcholine; whereas clinical experience (21, 25) shows that glutamic acid has an effect on *petit mal*, in which case, in turn, the slow potentials may be connected with decreased production of acetylcholine. The clinical results of administering glutamic acid to the feeble-minded (1, 27, 28) are as yet uncertain.

In this Department for Men, hyperammoniuria has previously been demonstrated, partly in patients with cramp, but also in patients with schizophrenia in its active stage (14, 15, 16, 19, 20). *Gjessing* (8, 9, 10), in his works on the phasic retention of nitrogen in periodic catatonia, has advanced the theory that there is intoxication by nitrogenous products of decomposition in these states. *Richter* and co-workers (22, 23), by a method devised by themselves, found no amines in normal blood or in the blood of schizophrenic patients. Applying

¹ Submitted for publication Dec. 1949.

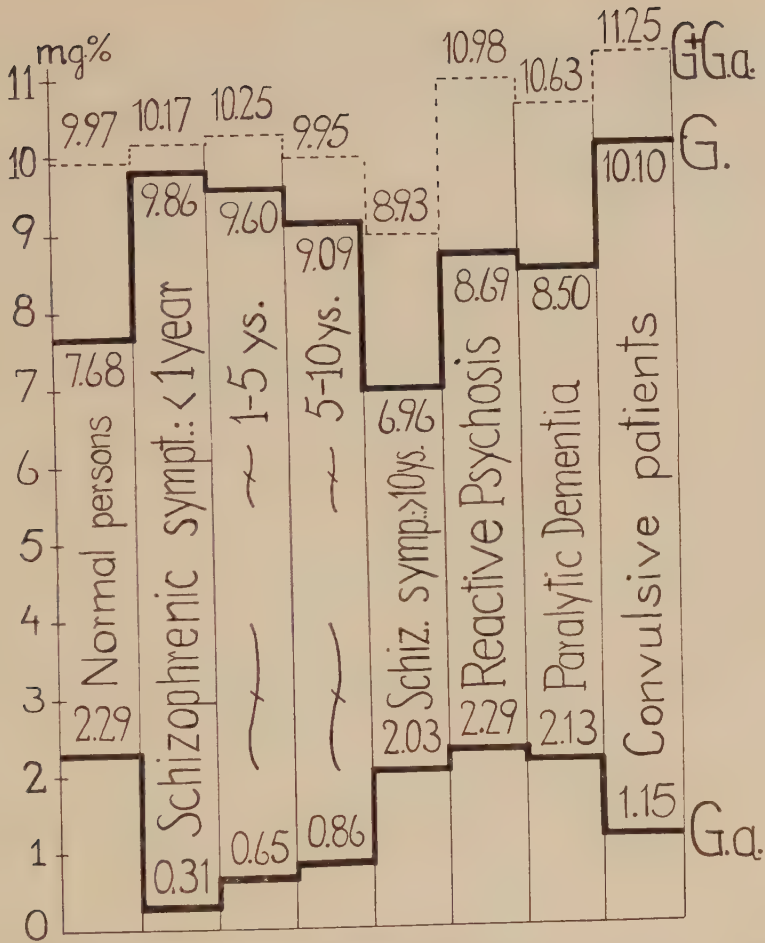
	Normal persons	Schizophrenia				Reactive Psychosis	Paralytic Dementia	Convulsive Patients
		sympt. < 1 yr.	sympt. 1-5 ys.	sympt. 5-10 ys.	sympt. >10 ys.			
Number of determinations	20	12	22	21	40	5	8	9
Glutamic acid								
mean	2.29	0.31	0.65	0.86	2.03	2.29	2.13	1.15
max.	3.16	0.55	1.74	1.64	3.77	3.22	3.25	2.44
min.	1.22	0.15	0.11	0.11	0.39	1.45	1.68	0.35
Glutamine								
mean	7.68	9.86	9.60	9.09	6.96	8.69	8.50	10.10
max.	9.83	12.63	12.21	12.00	8.87	10.51	11.98	12.60
min.	6.18	8.60	7.80	7.29	3.29	6.88	6.29	8.60
Glutamine + Glutamic acid	9.97	10.17	10.25	9.95	8.93	10.98	10.63	11.25

Contents of glutamine and glutamic acid in the plasma of a material of mental patients, and in 20 normal persons. The results are given in milligrams per hundred millilitres of plasma: mean values of the total number of determinations, besides maximum and minimum values ascertained.

a more sensitive modification of their method, we did not, at this hospital, succeed in demonstrating any difference in the content of amines in the blood of normal persons compared with that of schizophrenics (17). It was therefore decided to carry out determinations of the various amino acids, in order, if possible, further to elucidate the protein metabolism in patients with mental affections; as stated, it was decided to begin with determinations of glutamic acid and glutamine.

Krebs and co-workers (11, 13) towards the end of 1948 reported an enzymatic method for determining glutamic acid and glutamine. Their method has been tested in this department and a complete report is being prepared (*Astrup & Munkvad* (3)); it will also contain details of a normal material and tolerance tests in normal persons. Suffice it to mention that the main principle of the method is the enzymatic evolution of carbon dioxide from glutamine and glutamic acid in the presence of *Clostridium welchii* (strain S. R. 12), with measurement of the carbon dioxide evolved. Decarboxylation of glutamine is accompanied by the production of an equivalent quantity of ammonia (as determined by *Conway's* method).

By this method glutamic acid and glutamine were determined in the plasma of a considerable number of patients with mental affec-



Distribution of glutamine and glutamic acid in the plasma of a material of mental patients, and in 20 normal persons: in milligrams per hundred millilitres of plasma (mg./%). The figures are average results of the total number of determinations within each group. G. = Glutamine. G. a. = Glutamic acid.

tions, mainly schizophrenics, besides a few cases of manic-depressive and reactive psychoses, and convulsive patients. Besides, a control material is included, consisting partly of normal persons, partly of newer and older cases of paralytic dementia. All tests were made with the persons fasting; control tests, with the addition of known quantities of glutamine and glutamic acid to the plasma, were carried out at intervals. On each day of testing, moreover, patients from the different groups of affection were mixed, so that the same strain of bacteria should not be applied for the determination of glutamine

and glutamic acid in patients belonging to one single group; such procedure might, in theory, have caused a systematic error.

The results appear from the figure and the table. The schizophrenics are grouped according to duration of manifest symptoms (under 1 year, 1-5 years, 5-10 years, and above 10 years). The group of schizophrenics with symptoms of more than 10 years' standing, is mainly composed of chronic, inactive (deeply deteriorated) cases, but a number of cases in the active phase are also included. The variations observed in the glutamic acid figures within the various groups (the figure gives maximum and minimum results only) seem to be related to the degree of activity of the schizophrenic process at the time in question: pronounced activity appears to yield the lowest glutamic acid values. Further investigations of this question have been commenced.

At the time of writing, glutamic acid and glutamine have been determined in only 10-12 cases of manic-depressive psychosis. In pronounced manic states, glutamic acid values as low as 0.31 milligrams per hundred millilitres of plasma were found, whereas the figures reach normal levels when the mania has abated. Thus, low glutamic acid figures are not peculiar to schizophrenia in activity, although this is the state in which these preliminary investigations most constantly revealed low values.

In convulsive patients the low glutamic acid values are found in cases of recent origin. The glutamine level is remarkably high in the plasma as compared with the controls. Only active cases of schizophrenia approach these figures.

It should be stated here—as already mentioned in the introductory remarks—that we have in this hospital previously demonstrated hyperammonuria in the actual cases of convulsion and in the active stages of schizophrenia. Further investigations of the possibility of there being some relation between these states have also been planned.

SUMMARY

Determinations of glutamic acid and glutamine in the plasma of 150 patients with mental affections have shown decreased glutamic acid values in various psychotic states, especially in schizophrenia in the active phases, and in convulsive patients in a few cases.

Besides, increased glutamine values have been demonstrated in schizophrenics in the active phase, and in convulsive patients.

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THE CONTENT OF CELLS AND PROTEIN IN THE CEREBRO-SPINAL FLUID

Some causes of the highly varying accounts of the content of cells and proteins in the normal cerebro-spinal fluid, elucidated by the examination of some 1500 spinal fluids from cases of lumbar anesthesia. Further, a summary of the content of cells and proteins in some 12000 personally examined cerebro-spinal fluids (lumbar fluids).

By

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It is presumably a matter of common knowledge that the accounts of the content of cells and proteins in the normal cerebro-spinal fluid (CSPF) differ greatly. Thus the cell count varies from 0-1/3 (the content of cells in Fuchs-Rosenthal's counting chamber, capacity: 3.2 cu.mm) to 30/3, and the values given for the amount of protein range from 13 to 65 mg%. The chief cause of these differing values is, however, in each case the author's normal material, in so far as his figures are based on independent investigations and are not merely copied from other authors. "The normal material" in most cases consists of CSPF from patients with "psychopathies", skin diseases, or from patients with surgical (especially orthopedic) and medical diseases, in which the CSPF is assumed to be normal because it has not been possible at the clinical examination to find any symptoms of an organic neurological affection. For further details the reader is referred to previous works (14, 15).

Even if the author concerned originally had some doubts about the normality of his normal material he reckons with the values found and, what is worse, he does not as a rule detail the findings in which the content lies below the limit he regards as normal, but often merely says that the "CSPF is normal". Something similar applies to the authors who concur with his views. The consequence is that we have no know-

ledge of the small changes in the CSPF and their significance. In other words, we have here a vicious circle, where the "normal material" marks the view of the author concerned of the normal values of cells and proteins.

While, as far as I know, no author has previously found any fundamental difference in the content of protein in the spinal fluids of men and women, a Swedish author, Izikowitz (9, 10, 11), has recently thought it possible to show such a difference. He found a considerably larger content of protein in men (39.46 mg%: limits 13.72-65.20 mg%) than in women (30.99 mg%: limits 13.39-48.69

TABLE 1
Cell content in Fuchs-Rosenthal chamber 3.2 cu. mm

Diagnosis	0	1	2	3	4	5	6	7-10	11-15	15-30	30	total
Peptic ulcer	4	2	2	2	2							12
Gastric cancer	3	2		2	1							8
Cholelithiasis	7	11	4	2	1							26
Appendicitis	18	13	8	2		1						42
Herniae	19	28	11	11	3	5	1	2	3		1	84
Haemorrhoid.	17	10	5	2	1	1	1	1				38
Genit. femin.	27	20	4	5	2		1			1	1	61
Uro-genital	17	5	4	1	2	1				1		31
Prostate	20	16	7	5	1		1					50
Fract. extr. inf. etc.	26	18	5	7	4			2	1	1	1	65
Gangrene ext. inf.	11	13	5	2	3	1		1				36
Tumors	12	6	4	1	1	1						25
Variae	14	16	6	1	1			1	1			40
Total	195	160	65	43	22	10	5	7	5	3	3	518

mg%). He did not publish his views until 1930-32, and as far as I can see his statements on the normal limits are based on investigations made at the beginning of his work with the protein content of the CSPF, and to my knowledge they have not been repeated later. On various occasions from 1932 onward I have dissociated myself from his views, see my previous papers (14, 15). In my opinion we have a vicious circle here, too, which has led Izikowitz and his pupils (4-8, 16) further astray when they assume that there is a fundamentally higher protein content in the CSPF of men than in that of women and greater deviations in both sexes than hitherto assumed.

The cases of surgical affections in which operations have been performed under lumbar anesthesia date in the main from the years prior to 1932, that is to say, they predate or are contemporaneous

TABLE 2

Total protein in CSPV according to Roberts-Stolnikow-Brandberg-Bisgaard

Diagnosis	Dilution values									total
	3	4	5	6	7	8-10	11-15	16-20	20-	
Peptic ulcer	1	4	4	13	11	21	8	1		63
Gastric cancer			7	5	5	7	5	1		30
Cholelithiasis		3	26	27	23	16	4		1	100
Appendicitis		8	50	83	52	68	22	1		284
Herniae		2	8	19	23	55	40	5		152
Haemorrhoid.		1	9	16	19	36	21	1		103
Genit. femin.	1	8	27	39	27	30	6	2		140
Uro-genital		4	10	18	18	22	14	5	5	96
Prostate	1	2	5	17	16	41	32	7		121
Fract. ext. inf. etc.		1	13	12	17	35	15	1	2	96
Gangrene ext. inf.		1	5	9	9	19	21	2	2	68
Tumors		3	16	18	18	26	8		1	90
Variae	1	9	25	26	28	60	24	3	1	177
Total	4	46	205	292	266	446	220	29	12	1520

with Izikowitz' investigations. The tables given below of the cell and protein content in the CSPF (Tables 1 and 2) show the content in the various surgical affections. Cells were counted in 518 cases, and the protein content was determined in 1520 cases. The reason why the cells were not counted in all cases was that some of these spinal fluids were examined after the usual working hours and so the cell count could not be taken directly after the puncture.

In two groups, appendicitis and hernia, a closer analysis was made of the findings of cells and proteins. For protein see Table 3. This survey shows that there is a considerable difference in the protein findings in the two affections. In the case of the cells also there is

TABLE 3
Total protein (nitric acid values)

	4(3)-6	7	8	9	10	11	12	13	14	15	16	17	18	19	20-
Men:	63	30	11	22	12	6	6	3	2	2	1				
Appendicitis:															
Women:	78	22	14	2	7	1	2								
p. c.	50	19	9	8	7	2	2			3					
Men:	18	19	17	21	19	4	15	7	4	4	1	1	2	1	
Herniae:															
Women:	11	4	3	3	1	3	2	1							
p. c.	19	15	13	16	7	5	11	5			9				

a great difference, the hernia group showing more cells. The cell count within the two groups appears from Table 1.

As far as appendicitis is concerned it turns out that the temperature has no direct influence on the cell content, some very high temperatures being found (e.g. 39.7; 39.3) with cells 0/3, 1/3, but as far as can be inferred from the few observations, it is the duration of the disease that is of importance, for it is the cases which have lasted for some length of time that show a cell content of 2-5/3 cells, even though the temperature is low (5/3 c. at a temp. of 37.5). The same applies to the protein content which may be slightly increased in these cases.

The reason why the groups of appendicitis and herniae have been selected for comparison is that we have here a material which is comparable in number, age, and sex (see further Tables 3 and 4). As to sex, it appears from Table 3 that there is no fundamental difference in the protein content of the CSPF. The reason why there is a small preponderance of increased protein content in the men is a preponderance of chronic or recurrent cases of appendicitis. Something similar applies to the sex distribution in the hernia group, where changes in the hernia may be supposed to be more pronounced in men on account of greater physical exertion during work than in women.

TABLE 4

Age	-20,	21-30,	31-40,	41-50,	51-60,	61-
<i>Appendicitis:</i>						
Men:	24	65	37	22	7	3
Women:	19	64	19	9	7	8
<i>Herniae:</i>						
Men:	5	31	21	29	25	13
Women:		3	4	12	5	4

For the other groups in Tables 1 and 2 no close investigation has as yet been made of the individual cases in the respective groups, but random samples have shown similar conditions as in the appendicitis and hernia group as regards the reason why some few instances show a slight increase in the protein content of the CSPF.

As a slight contribution towards the explanation of the CSPF changes in hernia a single section from each of a total of 24 sacks of hernia was examined. In 10 of these, mostly old hernial sacks, only

fibrous changes were found in this section, but in the rest the findings were either signs of inflammation with round cells and plasma cells, or signs of endothelial proliferation, sometimes both combined (see the illustration in *Bibliotek for Læger 1936*, p. 214). From our experience of the changes in the CSPF in appendicitis, where it was especially in chronic or recurring cases that changes occurred in the CSPF, it would seem possible that the inflammatory changes in hernia have a share in the changes in the CSPF. If this is so, the inflammatory changes in gastric ulcer, in which, even in chronic and apparently healed cases, pronounced inflammatory changes are found, perhaps play a part in the frequent changes in the CSPF, and this may also apply to changes in other chronic inflammatory conditions in the abdomen, e.g. in cholelithiasis and salpingitis, but a close analysis of these affections has not yet been made.

If we are to explain why, in certain instances, slight pathological changes may occur in the content of cells and proteins in the CSPF, the easiest method will perhaps be to survey the ways in which pathological changes arise in the CSPF. There may be (1) inflammatory processes in the meninges and the central nervous system, allergically conditioned changes being included; (2) haemorrhages or necroses as a consequence of vascular affections or traumata in the central nervous system or its membranes with sequelae after such processes; (3) sequelae of pressure with a changed blood circulation and exudation of serum, as a rule owing to obstructed passage from the veins, e.g. in changes owing to tumours in the central nervous system, especially on the base of the cerebrum or in or around the spinal cord. Another example of increased protein owing to pressure is in my opinion afforded by the great protein changes in acute polyradiculitis. In monoradiculitis, too, a slight increase in protein may be found, and with respect to the changes in certain surgical and medical affections it will be natural as a working hypothesis to consider changes in the nerve trunks leading from the spinal cord to the pathologically changed area as the cause of the increase in protein. It would be natural to examine these nerve trunks, e.g. nervus vagus, by extirpation of part of the latter, as is done in some cases in the modern treatment of gastric ulcer. It is a well-known fact that certain affections of the central nervous system may be accompanied by gastric ulcer; it is possible that the changes in the CSPF may be particularly marked in such cases, even though it is hardly probable. However, it would perhaps repay the trouble to examine the central nervous system in a small series, especially the spinal cord with the roots at the zone of entry as well

as the nuclear areas of nervus vagus and the hypothalamic region from patients who have died from gastric ulcer. It would likewise presumably be of interest to examine in a similar way, whenever occasion offered, the corresponding areas from other affections when there was a change in the CSPF. Such investigations would of course have to be checked by examination of suitable normal material. Further, it would perhaps be convenient to ascertain whether changes in the CSPF could be demonstrated experimentally in animals in which a chronic inflammation had been induced, if this be possible, in the abdomen or the extremities.

Prior to a discussion on what values should be accepted for the content of cells and protein in normal CSPF it will no doubt be appropriate to give a summary of the findings in about 12000 CSPF's. I have made these investigations personally, and in 85-90 % of the cases without the slightest knowledge of the affection of the patient concerned. In the remaining 10-15 % of the cases of CSPF from lumbar anesthetics I knew the diagnosis but not the course of the affection in question. For comparison the findings in 1787 cases (x) from the Neuro-Medical Department of the Rigshospital have been given where the analyses have been made without the least knowledge of the disease on my part. These cases consist in the main of chronic

TABLE 5
Cell content in Fuchs-Rosenthal Chamber, 3.2 cu.mm.

	0	1	2	3	4	5	6	7-10	11-15	>15
p. c.	14	27	13	7	5	4	3	6	4	17
(x)	37	20	14	8	5	3	2	4	2	5

Total Protein. Nitric Acid Values. Dilution Values.

	4	5	6	7	8	9	10	11	12	13	14	15-20	21-40	>40
p. c.	3.5	8	11	11	8	8	13	5	5	3	2	12	7	3.5
(x)	2	4	8	9	14	16	10	1	5	2	4	12	8	5

Globulin. Ammonium Sulphate Values. Dilution Values.

	0	0(1?)	1	2	3	>3
p. c.	63	16	8	4	3	6
(x)	29	28	30	6	2	5

organic nervous affections with comparatively few syphilitic diseases. The findings are given in per cent. See Table 5.

I must at once point out that it is not my intention to boost any particular limit for the normal finding of cells and protein, but merely to emphasise that, since the opinions on the normal limit are so divergent, it is absolutely necessary to state accurately what has been found and not merely say that the CSPF was "normal" if the findings lie just under or on the verge of the limit considered normal by the observer.

If we are to form an opinion as to the question of normal limits the special position occupied by the CSPF should first be kept in mind. Normally it is thus bounded that the boundaries are impermeable to colloids. As far as the CSPF is concerned we may refer the reader to the very numerous publications on the blood-spinal fluid and the blood-brain barriers. For that reason it is probable that the cell and protein content is normally very low and so it is improbable that normally there should be any decisive fundamental difference in the CSPF's of men and women. The difference which Isikowitz and his pupils have thought it possible to point out is in my opinion due to other factors, especially, as already mentioned, the different life conditions of the two sexes.

Of other reasons for assuming a normally very low content of cells and proteins in the CSPF there is, as stated in previous papers, the circumstance that in subjects who after examination at the hospital do not present any symptoms of disease that may be supposed to affect the CSPF, a very low cell and protein content is found (0.1/3 cells, globulin 0, total protein 3-6 according to Bisgaard's method), while if the individual in question suffers from a disease which may be supposed to affect the cell and protein content of the cerebrospinal fluid, we find changes, even though in most cases they are so small that, as stated above, they are usually considered to lie within normal limits. My argument, however, is that there would be no possibility of demonstrating such small changes if the normal content were not still lower.

Another argument is that in affections of the central nervous system pronounced changes often occur in the incipient and early stages of the affection, while, when the affection either spontaneously or owing to treatment is cured or passes into a chronic stage, we see that these changes disappear either wholly or partially so that there is now quite a normal or an only slightly changed CSPF. As an example may be mentioned that Dattner by a vigorous penicillin therapy in a case of dementia paralytica with originally very strong

positive reactions was able to reduce the total protein to 13-24 mg%, i.e. quite normal conditions. Assuming a considerably higher normal content of proteins Izikowitz and his pupils must necessarily work with individually differing protein contents, which seems to me quite improbable.

The determination of protein was made according to the method of Bisgaard, which is assumed to be known. This method acts with great accuracy in cases of normal and slightly increased pathological protein contents, as has been shown by a comparison with other methods. With higher protein content it is less accurate like other clinical methods for the determination of protein. With normal and slightly changed CSPF the dilution values found may be converted into protein given in mg% by multiplying the dilution value by 4 to 4.5, but with a greater increase in proteins and especially with increased globulin the constant is much lower, at 1.5 to 2, as shown in previous papers. A Pandy reaction is also employed, as well as a quantitative determination of globulin according to the method of Nonne-Apelt. In cases of chronic, particularly syphilitic affections after treatment, it is often seen that there is a relative preponderance of globulin as compared with albumin. This was realised already by Bisgaard (1) and recently Kafka-Samson (12) in particular, have by their method shown the importance of pointing out this fact.

With regard to the technique of the investigation the reader is referred to previous publications (14, 15).

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ENCÉPHALOPATHIES ET TROUBLES CARACTÉRIELS À LA SUITE DES BRÛLURES CHEZ L'ENFANT

Par

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Parmi les facteurs étiologiques, relativement peu étudiés, des encéphalopathies ou des perturbations caractérielles des enfants, les brûlures sérieuses occupent une place qui mérite d'être soulignée attentivement. En parcourant la littérature, nous avons trouvé peu de renseignements sur ce sujet. On semble s'intéresser — à juste raison d'ailleurs — aux troubles neuro-psychiques que présentent ces enfants au cours des heures et des jours qui suivent l'accident, et l'on semble se désintéresser de leur avenir neuro-psychologique.

Ayant observé quelques faits de troubles tardifs, nous les résumerons en les commentant à la lueur des données mises en évidence par les auteurs qui nous ont précédés dans cette voie.

Toutefois, dans la discussion des cas, il est juste de tenir compte du rôle adjuvant joué par d'autres facteurs, sans lesquels, peut-être, la brûlure seule n'aurait pas provoqué des dégâts tardifs.

Voyons d'abord ces faits:

Obs. no. 1. A.D. 5 ans 2 mois, est amené pour un retard de la croissance et un langage considéré comme « trop puérile » pour son âge et parfaitement incompréhensible.

Affectueux à la maison, il ne fait pas de difficultés alimentaires. Sait s'habiller seul, mais est très lent.

Historique : né à terme par forceps, il a été très cyanosé ; on a dû le ranimer pendant environ 30 minutes. A crié ensuite. Au sein pendant 9 mois. Premier développement (dentition, marche et propreté des sphincters) relativement normal. Premiers mots entre 10 et 12 mois. Les parents précisent que, de ce point de vue, tout était normal jusqu' à 24 mois quand il se brûla avec un fer à repasser. Terribles atteints : la main gauche et l'hémithorax correspondant. Il était tombé sur le fer chaud et sa maman n'a pu le secourir que plusieurs instants après. On le soigna pendant 3 semaines. Or, environ 50 jours après l'accident, sans que rien d'anormal soit intervenu, l'enfant a été trouvé inconscient, l'écume aux lèvres, ronflant et ayant perdu des urines. Des crises comitiales typiques ont, par la suite,

été observées à 2-3 reprises seulement. A l'âge de 5 ans, il fit de nouveau, sans cause nette, des crises convulsives généralisées à l'hémicorps et à l'hémiface droits.

Examen : constitution moyenne ; masses adipeuses et musculaires peu développées. La thyroïde n'est pas augmentée de volume. Les organes génitaux normaux pour l'âge de l'enfant ; crémastériens vifs. L'examen neurologique est entièrement négatif. Pas de signe de Chvostek, ni buccal. Pas de troubles trophiques. Pas d'énurésie, ni d'encoprose.

Morphologiquement, nous notons que le crâne est petit et l'on palpe la suture métopique (sous forme d'une véritable crête). Taille : 99,5 cm, au lieu de 105 et poids : 15 kg, au lieu de 18,5 kg ; donc, retard staturo-pondéral.

Psychologiquement, cet enfant se comporte comme un bébé de 3 ans ; il n'est pas capable de faire la moindre petite phrase.

Commentaire : Cet enfant de 5 ans 2 mois, est vu pour un retard staturopondéral d'une part et de son langage d'autre part. Il n'est pas sourd ; il n'est pas, apparemment, un oligophrène. Quelle est la cause de son état actuel ?

Deux facteurs peuvent être invoqués. En premier lieu, les circonstances de *sa naissance*. Nous avons vu, effectivement, qu'il s'agit d'un traumatisme obstétrical ; il est né par forceps, cyanosé ; on a dû le ranimer longtemps. Or, cet élément étiologique se trouve souvent dans les antécédents des enfants dont le langage est retardé ou défectueux. Dans une monographie sur le profil neuro-psychologique des traumatisés de naissance (353 enfants forcipités et asphyxiés), nous avons montré que le retard du langage est de l'ordre de 59,25 %. Par ailleurs, 43 sur 208 enfants (soit 12,25 %) ne parlaient pas encore au moment de notre enquête.

Le deuxième facteur, le facteur *dominant* dans notre cas, est l'accident dont nous avons fait mention. *Brûlure grave*, car elle fut suivie, environ 50 jours plus tard, de convulsions répétées, typiques. Or, chez cet enfant l'installation des premiers mots fut normale (remontant à l'âge de 10-12 mois). Son langage normal jusqu'à cette date, ne fit, dans la suite, aucun progrès ; plus encore, les parents prétendent même, qu'il s'agit d'un *regress* plus ou moins évident.

Il est difficile d'accuser exclusivement le traumatisme obstétrical. En effet, on ne voit pas pourquoi cet enfant, dont la fonction verbale s'est installée à temps, fait des troubles portant sur une fonction qui a déjà donné une preuve tangible de son intégrité initiale. On doit, donc, incriminer essentiellement la brûlure, tout en tenant compte, comme nous le verrons du *rôle favorisant possible*, joué par le traumatisme cérébral précédent. En effet, il est possible d'admettre que le terrain neurologique fragile a peut-être « facilité » l'apparition, lors de la brûlure, des crises convulsives.

En d'autre termes, on peut se demander si, dans notre cas, il ne s'agit pas d'une sorte de *comitialité réflexe*, la brûlure déclenchant des crises sur un cerveau présentant des micro-lésions cicatricielles antérieures.

Le fait suivant semble plaider en ce sens.

Obs. no. 2. Y.J. 9 ans, est vu pour des crises convulsives et oligophrénie. Cinquième de 6 enfant, il est né à terme et s'est développé normalement jusque vers 9 mois, lorsque, sans cause apparente, il fit des crises convulsives généralisées avec révulsion des globes, mouvements tonico-cliniques, relâchement des sphincters. Ces crises se sont répétées d'ailleurs, avec des intervalles plus ou moins importants jusqu'à l'âge de 6 ans.

A l'examen, son développement est pratiquement normal (taille 119 cm, poids 24 kg). Masses adipo-musculaires bien développées pour son âge. Squelette normal. Crâne : 48,5 cm. Suture métopique palpable. Dentition normale. Chvostek III bilatéral. Organes génitaux normaux, thyroïde non palpable. Au point de vue neurologique hémiparésie spasmodique gauche, avec Babinski ; pas de troubles trophiques notables. Pupilles égales, régulières et réagissant normalement à la lumière et accommodation. Au point de vue psychologique : coléreux, instable, incapable de suivre la classe, débile mental (au test de Binet-Simon).

Un EEG (dr. H. Gastaut) montre des tracés formés par un rythme alpha à 11-12 c/s, légèrement prédominant dans les régions occipitales, où il est d'amplitude majeure. Il existe quelques bouffées d'ondes thêta à 6-7 c/s à tendance synchrone. Dans les régions occipitales, quelques images d'un rythme delta à 4 c/s. L'hyperpnée n'altère pas notablement le rythme alpha. En somme, ces tracés apparaissent sensiblement normaux. Absence de signes nets de comitialité.

Or, du point de vue qui nous intéresse ici, l'enfant présente, au niveau de la région pectorale, surtout à gauche, et s'étendant en un vaste placard qui occupe aussi la surface interne et moyenne du m. sup. g., une énorme cicatrice nacrée, souple, séquelle d'une brûlure avec du café brûlant. Cet enfant, qui avait une crise toutes les 10-15 jours environ, a présenté au cours des 15-20 heures après son accident, une série de crises ayant nécessité l'application d'un traitement sérieux comme s'il s'agissait d'une menace d'état de mal.

Commentaire : Chez cet enfant qui fait des crises comitiales depuis l'âge de 9 mois (la cause nous a échappé, mais nous avons des sérieuses raisons de suspecter la syphilis des parents) et qui les voit survenir toutes les 10-15 jours, une brûlure sérieuse a provoqué une série paroxystique dans les heures qui suivirent l'accident. En somme, les choses se sont, probablement, passées, comme si à la faveur de la préexistence de lésions cérébrales, minimes, les troubles engendrés par la brûlure (nous en parlerons plus loin) ont suffi pour déclencher les paroxysmes.

Il serait intéressant de rechercher, attentivement, des antécédents de ce genre, chez des petits comitiaux.

Mais, voici encore une observation clinique dans laquelle la brûlure a, de toute évidence, joué un rôle dominant, comme dans l'obs. no. 1.

Obs. no. 3. R.M. 6 ans 3 mois, est examiné pour « retard mental ». Son père, un alcoolique « nerveux », est lui-même, fils d'un alcoolique invétéré. La mère est bien portante, sauf une note d'hyperthyroïdie. Les deux parents ne présentent, cependant, pas des signes de syphilis nerveuse.

Né par forceps (appliqué à *deux reprises*), R. a été très cyanosé et n'a crié que plusieurs minutes après. Il a pris le sein seulement le 3-e jour après sa naissance. A mis tard (?) sa première dent ; a marché vers 20 mois et a parlé vers 5 ans, de façon acceptable. Enurésie jusqu'à 3 ans 6.

Rien de notable dans ses antécédents jusque vers 18 mois quand, par inattention des siens, il se brûla avec de l'eau bouillante. Parties atteintes : le menton, la région sous-mentonnaire, le cou, le thorax et la partie interne du bras droit. Au début, la brûlure ne paraissait pas grave, mais le *septième jour* après l'accident, l'enfant a fait des convulsions généralisées (raideur et mouvements cloniques, révulsion des globes, écume à la bouche). Ces crises se sont répétées plusieurs fois *le même jour et dans la nuit*. Jamais plus de crises depuis cette date, malgré les maladies éruptives ultérieures (rougeole, coqueluche, oreillons).

Actuellement : comportement peu affectueux ; l'enfant frappe ses amis, il est instable, très turbulent.

Examen : développement adipo-musculaire satisfaisant. Taille : 115 (au lieu de 105), poids : 28 kg (au lieu de 21). Présente une rétraction, avec enfoncement médio-thoracique bilatéral qui réalise une forme fruste de thorax en entonnoir (absence de ce stigmate chez ces parents). Pas de laxité articulaire. Crâne : bosses parétales légèrement accusées. Circonférence : 53 cm. Squelette : normal. Dentition : normale. Thyroïde non palpable ; organes génitaux normaux. Système nerveux : rien d'anormal. Pupilles égales, régulières et contractiles à la lumière et à l'accommodation.

Profil mental (Binet-Simon) : âge mental de 4 ans 3 mois, soit débilité mentale (Q.I. 0.68). Son graphisme (test de « bonhomme ») est d'un niveau très bas.

Commentaire : Il s'agit, en somme, d'un enfant présentant un retard dans le développement mental avec instabilité psycho-motrice ; la parole, défectueuse encore, s'est installée tard, l'acquisition du contrôle des sphincters fut aussi retardée. Quelle est la cause de ces troubles ?

Nous n'avons pas de raison de suspecter l'infection syphilitique. Par contre, il est indéniable que l'*alcoolisme* du père et du grand père paternel, ne doit pas être oublié. Cette tare peut expliquer, à elle seule, l'instabilité psycho-motrice de l'enfant. Mais est-elle aussi la cause de la déficience mentale du sujet ? On pourrait, à la rigueur l'affirmer. Or, dans les antécédents de cet enfant d'autres éléments étiologiques sont à envisager.

Comme dans l'observation no. 1, il s'agit d'une *naissance traumatique* (forceps) ; ensuite, élément qui saute aux yeux, c'est la *brûlure* survenus à l'âge de 18 mois. La gravité de l'accident est soulignée par l'apparition de convulsions généralisées à la fin de la première semaine. Crises qui se sont répétées plusieurs fois durant la même journée et la nuit.

S'il n'est pas douteux que cet élément étiologique a joué un rôle

primordial, il importe aussi de noter le rôle de la tare éthylique et de la naissance traumatisante.

Parfois, sans avoir entraîné l'apparition de convulsions, la brûlure peut être trouvée comme unique *élément étiologique significatif* capable d'expliquer (même partiellement) des troubles caractériels ou du comportement. Voici, en effet, une observation plaçant dans ce sens.

Obs. nr. 4. Garçonnet de 3 ans, dont l'âge mental est d'un enfant d'à peine 2 ans. Né à terme d'un père âgé (68 ans) et d'une mère de 29 ans plus jeune, cet enfant s'est, au début, développé normalement. Mais, actuellement encore, il ne parle pas bien, est énurétique et nous est amené pour : colères violentes, instabilité, méchanceté envers les animaux et bris des objets, qu'il rencontre dans son entourage.

Examen : développement somatique retardé (taille 89 cm, au lieu de 96) ; dentition normale. Squelette normal, viscères aussi. Examen neurologique négatif. Déjà, au début de l'examen, l'enfant hurle et s'oppose violemment à nos manœuvres. C'est à la suite de toute une série de stratagèmes que nous avons pu le déshabiller et l'examiner attentivement.

Quelle est la cause des troubles caractériels de cet enfant ?

Après avoir éliminé la syphilis, l'éthylisme ou des déterminations encéphaliques para-infectieuses, nous avons cru raisonnable d'invoquer l'accident suivant qui se situe à l'âge de 18 mois environ : en effet, ce sujet a fait une chute contre un poêle brûlant et provoqua, en même temps, le renversement d'une casserole d'eau bouillante. La double brûlure porta sur la région crânienne. Actuellement, l'enfant porte une cicatrice nacrée qui siège sur la ligne parasagittale droite, longue de 6 cm. et large de 2-3 cm.

Commentaires : Dans le cas que nous venons de résumer, il s'agit de troubles caractériels chez un enfant dans les antécédents, duquel, après avoir éliminé d'autres facteurs étiologiques (exogènes), il est raisonnable de faire état du rôle possible d'une brûlure survenue très tôt, c'est à dire au cours de la première enfance.

Après l'exposé des faits qui sont à la base de notre présent mémoire, nous devons nous demander si les tableaux encéphaliques et les troubles caractériels des anciens brûlés (enfants surtout) sont ou non fréquents.

Si l'on parcourt la littérature pédiatrique des brûlures, on lira comme vient de le montrer dans un important travail *B. Morrison, 1947*—que souvent les brûlures importantes entraînent, entre autres symptômes généraux, des manifestations du côté du système nerveux. Il s'agit, surtout, d'un état de somnolence, d'agitation avec soubressauts, enfin de convulsions, qui surviennent plus ou moins tôt, après l'accident. En ce qui concerne, tout particulièrement, les convulsions, l'auteur anglais cité, les note 5 fois sur 31 cas, soit 16 % ; un chiffre non négligeable. Mais, dans ce travail, il s'agit uniquement du tableau

clinique aigu. Aucune mention n'est faite quant à l'avenir neuropsychologique de ces enfants.

Sur plusieurs centaines de syndromes encéphalopathiques infantiles que nous avons eu l'occasion d'étudier au cours des dernières années, nous avons eu rarement l'occasion, comme dans les cas ci-dessus analysés, de faire intervenir le rôle dominant ou adjuvant d'une brûlure. Pourtant, nous sommes très attentifs et très minutieux dans nos recherches anamnestiques.

Dans la littérature médicale mondiale, nous avons trouvé les contributions suivantes que nous voulons résumer.

En 1928, *F. Kruse*, a relaté le cas d'un nourrisson de 14 mois qui, à la suite d'une brûlure de 2^e degré, a présenté une amaurose s'accompagnant d'hydrocéphalie progressive et d'une altération importante du comportement. Seule l'hydrocéphalie regressa ; les troubles du comportement persistèrent.

L'observation d'un enfant de 8 ans, relatée par *J. H. Globus* et *M. B. Bender* (1936) concerne un fait d'encéphalite toxique consécutive à une brûlure étendue.

De son côté, *N. Roth* (1941) a publié le cas d'une fillette de 8 ans, victime d'une brûlure sérieuse qui avait entraîné, le 20^e jour, des convulsions généralisées. Par la suite, cet enfant devint irritable et son langage subit une régression nette. De plus, on nota des mouvements de type choréo-athétosique de la main droite. L'encéphalographie mit en évidence une hydrocéphalie marquée, portant sur les ventricules latéraux et sur le 3^e ventricule. En plus, il constata une zone d'atrophie corticale fronto-pariétale.

En confrontant nos faits avec ceux des auteurs que nous venons de citer, nous constatons que c'est à la suite d'un véritable « intervalle libre » qui peut aller de quelques jours à 50 jours, que peuvent apparaître des crises convulsives généralisées, expression d'une atteinte cérébrale (cortico-sous-corticale).

Quant aux troubles cliniques, ainsi que nous l'avons vu plus haut, ils portent tantôt sur la sphère visuelle (amaurose : *Kruse*), tantôt sur la parole (alexie, aphasie, agraphie : *N. Roth, nous-mêmes*), tantôt sur la motricité élémentaire (athétose : *N. Roth*), tantôt, enfin, sur le développement psycho-moteur, intellectuel et sur le caractère ultérieur (*Kruse, N. Roth, nous-mêmes*).

Quelle est la pathogénie de ces complications tardives ? Comme pour les autres complications des brûlures, on a invoqué le rôle des toxines élaborées *in situ*, qui diffusent dans l'organisme et irritent les centres nerveux supérieures. Cette idée est réfutée par *Kruse* qui incrimine l'intervention d'un *oedème cérébral*, plus ou moins important. Par ailleurs, l'existence de l'intervalle libre, autorise également

N. Roth de rejeter l'hypothèse d'une intoxication *strictiori sensu*. Ajoutons, enfin, que cette conception est soutenue, avec des *preuves anatomiques* à l'appui, par B. Morrison, qui a pu étudier, de ce point de vue, 7 enfants décédés du fait des brûlures.

Mais peut-on affirmer que *seule* la brûlure accidentelle, suffit pour déclencher l'ensemble des troubles tardifs dont nous venons de donner la description ? N'est-il pas alors étonnant de constater la relative *rareté* des tableaux cliniques neuro-psychiques séquellaires en face de la *grande fréquence* des brûlures dont sont victimes les enfants ?

Quelle peut, donc, être la cause de cette constatation cliniquement indéniable ?

A cette question, les observations personnelles ci-dessus résumées, semblent proposer une explication possible. Nous avons, effectivement, l'impression que seulement les enfants *dont le cerveau a déjà subi une atteinte pathologique* (toxique ou infectieuse, ou les deux à la fois) ont des chances de présenter des accidents cérébraux ou cérébro-psychiques précoces ou tardifs. C'est sur des cerveaux présentant des lésions vasculaires ou vasculo-parenchymateuses préalables, que l'oedème cérébral et les troubles hémodynamiques engendrées par la brûlure, provoquera des dégâts suffisamment importants, suffisamment durables, pour entraîner à la fois des troubles paroxystiques immédiats et des manifestations tardives.

Cette conception *dynamique poly-étiologique*, nous l'avons défendu pour la meilleure compréhension des mécanismes pathogéniques qui sont à la base de la plupart des syndromes encéphalopathiques, toxico-infectieux, des enfants.

Les recherches clinico-pathologiques de l'avenir, auront pour mission de vérifier et voir jusqu'à quel point notre façon de voir correspond, ou non, à la réalité des faits.

R É S U M É

L'exposé de quatre observations, permet à l'auteur de discuter le problème, relativement négligé, des états encéphalopathiques infantiles consécutifs aux brûlures. Le rôle que joue cet élément étiologique est incontestable, mais, selon l'auteur, il faut savoir faire la part à d'autres facteurs « adjuvants », comme les infections ou intoxications des géniteurs ou le traumatisme obstétrical. C'est, effectivement, sur ce terrain fragilisé au préalable, que les perturbations hémodynamiques et l'oedème cérébral provoqués par la brûlure, engendrent ultérieurement, les troubles paroxystiques ou définitifs que présentent ces enfants.

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CLEIDOCRANIAL DYSOSTOSIS

(One case)

By

ARDIS STORM-MATHISEN and ARNE ENGESET

Cleidocranial dysostosis is a rare anomaly, which mainly involves different parts of the skeletal system, for preference the skull and the clavicles.

This anomaly was described first in 1765 by *Martin*, but was named in 1897 by *P. Marie* and *Sainton*: "Dysostose cleidocrânienne héréditaire".

In Norway the anomaly has been recorded previously in 1920 by *Yttri* and in 1934 by *Evensen*. *Eltorm* presumes that about 200 cases have been published in the world literature up to 1945.

Our case was discovered by mere chance, as was the majority of the other cases reported.

A 17-year old boy presented himself at the neurological outpatient department of the University Hospital because of periodical pain in the forehead and in the back of the head when suffering from colds and after exertion. He also complained of periods of poor audition and aphasia.

Clinical examination: The shape of the skull is almost square (transverse diameter 30 cm—longitudinal diameter 32 cm, circumference of glabella—occipital protuberance 58 cm). The parietal and frontal tubera are more prominent than usual. The forehead is steep and high-domed. The cranial bones are strikingly large as compared with the facial bones, the face appearing small. The outer angle of the eye is at a lower level than the inner one, and there is a good distance between the eyes. There is *atresia of both external auditory canals*.

The arch of the palate is high and pointed. In the upper jaw there are two molars posteriorly on the left side and one rudimentary tooth opposite on the right side. In the lower jaw there are nine deformed, irregularly placed teeth.

The usual clavicular bones cannot be palpated. The patient is easily able to bring both shoulders to the front so that they touch. By this movement distinct scapula alatae is observed. The shoulder blades are deformed and unusually small. The chest has a long and narrow appearance, and the anterior surface continues straight over into the anterior surface of the throat, without the usual clavicular protuberance. The nape of the neck is short and broad, the lateral outline of the trapezius muscle being more oblique than usually. An almost angled kyphosis of



Fig. 1.

Note movement and position of shoulders.

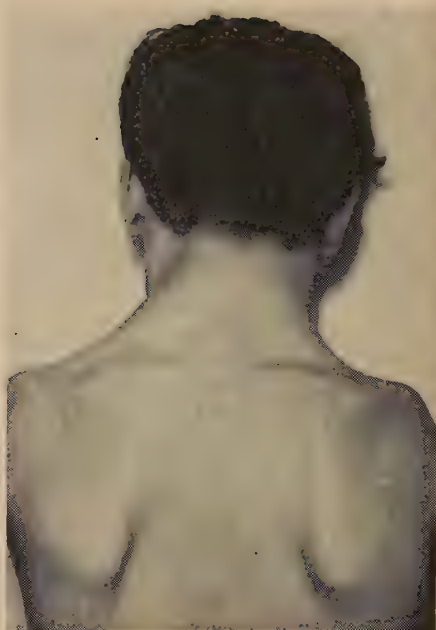


Fig. 2.

Scapula alatae.

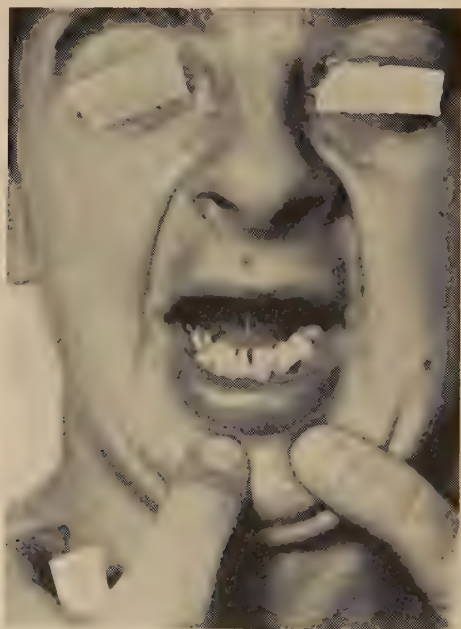


Fig. 3.

In the lower jaw are seen 9 deformed, irregularly placed teeth.

the upper thoracic spine, a right-convex lumbar scoliosis, and a left-convex thoracic scoliosis are seen. The pelvis appears high and compressed from side to side. The patient is distinctly knock-kneed. Toes and fingers are elongated. The muscular power is good.

Normal blood values, especially with regard to calcium and phosphorus (10.6 and 4 mg %), fasting blood sugar normal. Sedimentation rate 5 mm in one hour, the Wassermann test negative, blood pressure 110/65. Urinalysis shows normal conditions.

Apart from the difficulties of speech (due to the teeth) and the deformities, the neurological condition is normal.

Normal intelligence. The patient has passed through the seven forms of preparatory school with satisfactory marks. He is now working as a printer. The patient takes part in ordinary sports and athletics, with average performance.

X-ray examination: Numerous Wormian bones and corresponding divided sutures between the bones of the skull. The sutures are everywhere strikingly loose. Distinct basilar impression (especially in the sellar region and the nearest surroundings, which protrude into the skull). There is no pneumatization of the temporal bones, and the structure of the bone is sclerotic. The accessory sinuses are only slightly developed, the frontal sinus entirely absent. The distance between the orbitae is somewhat large. The facial bones are strikingly small. The forehead is domed, the back of the head protruding somewhat. *The clavicles are entirely absent.* There is thoracolumbar kyphoscoliosis. The vertebrae are somewhat irregularly shaped, and corresponding to the clinically demonstrable, almost angled kyphosis in the thoracic part they are nearly wedge-shaped (lowest anteriorly). The marginal borders are irregular and non-ossified (the patient is 17 years old).

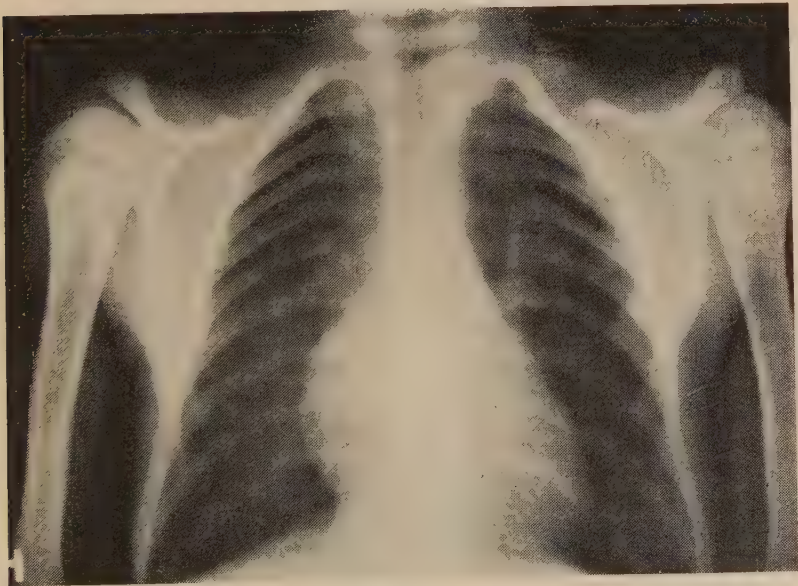


Fig. 4.

Bilateral total absence of the clavicles. The coracoid process is undeveloped.
The glenoid cavity is abnormal.

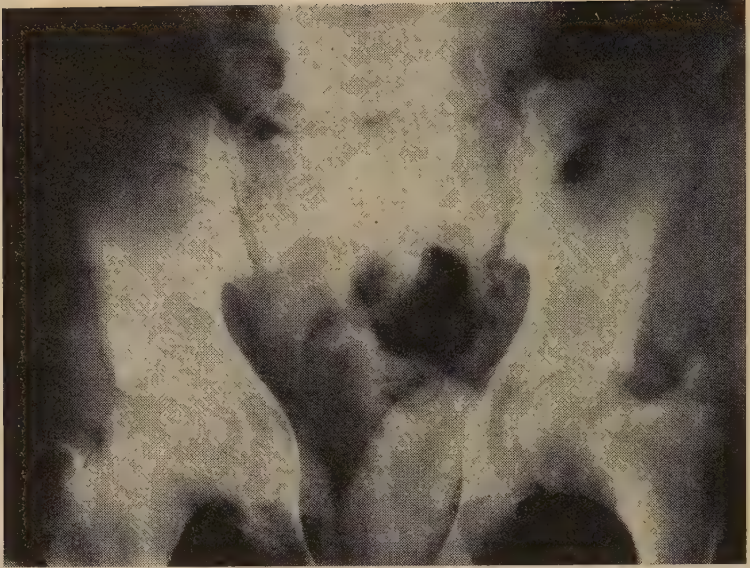


Fig. 5.

Deformity of the pelvis. Both acetabular regions protrude into the pelvic cavity. The medial parts of the pubic bone and the ischiatic bone are undeveloped. The obturator foramen is observed to be characteristically open medially. The deformity is easily seen, *but the absence of bone in the symphyseal region is remarkably easy to overlook.*

The changes are reminiscent of those in juvenile kyphosis of Scheuermann. Spina bifida is present in almost the entire length of the spine. The processes on the 7th cervical vertebra are larger than usually, and rudiments of a cervical rib are seen on both sides. The pelvic inlet has a trefoiled shape, no doubt *due to deficient development and ossification of the medial parts of the ischiopubic bones, in that the medial part of the obturator foramen is absent, which is a characteristic feature of this anomaly.* There is *coxa vara* on the left side. As a more unusual finding, however, there is *coxa valga* on the right side. The shoulder blades are small and poorly developed, especially the glenoid cavity. The coracoid process is hardly visualized. The long tubular bones are coarse, and this is the case also with some of the metacarpal bones. Hands and feet are markedly long, with no other anomalies.

The diagnosis in a typical case like this should be no problem, neither clinically nor radiologically. This case presents the four cardinal symptoms enumerated by *Valentin*, viz.

- (1) Unilateral or bilateral displacement of the clavicle.
- (2) Anomalies of ossification in the skull and in the dental system.
- (3) Anomalies in the pelvis and in the proximal part of the femur.
- (4) Anomalies of fingers and toes.

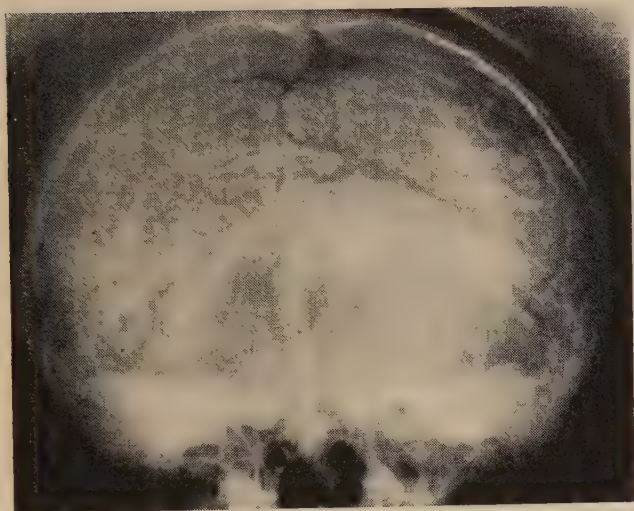


Fig. 6.
Basilar impression (platybasia).

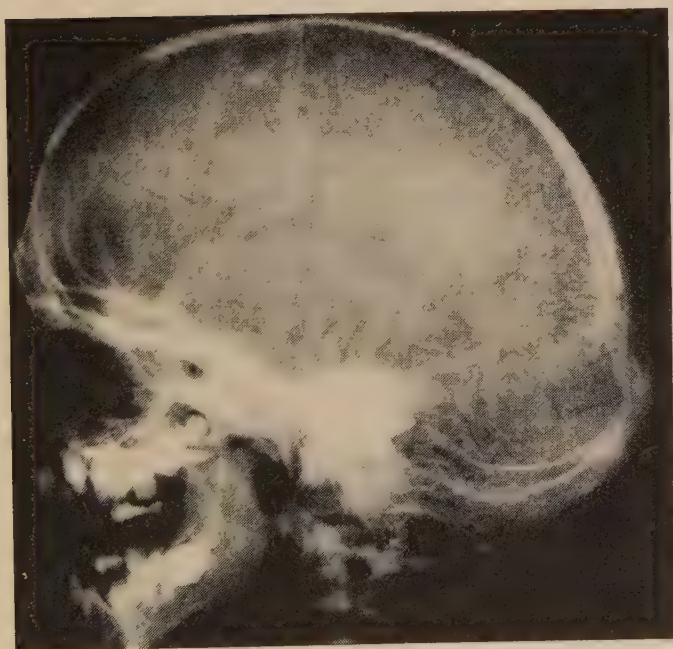


Fig. 7.

The pneumatic system poorly developed. Protruding posterior skull cavity. Slight basilar impression. Numerous Wormian bones. The sutures are remarkably open.

In the present case changes are found corresponding to all these groups. It is of special interest to otologists that bilateral atresia of the external auditory canal may be found together with the previously described changes in the cellular system of the skull, though with normal hearing.

Etiology: Most investigators agree that the disease may be *hereditary*, which seems to appear from larger materials published. In the family of our patient only a 4-year old brother has been examined satisfactorily. He died from cerebellar medulloblastoma. The skull in his case demonstrated normal conditions apart from the signs of increased intracranial tension. Other members of the family were unwilling to submit to X-ray examination.

Brauer claims that the anomaly may be found anywhere in the presence of mesenchymal tissue. He also holds that these changes may depend upon a *mutation* which electively may involve the pre-formed osseous system. Other investigators are of the opinion that *infections during pregnancy* may play a rôle. (There are many other opinions also on this question, which are hardly of interest in this brief survey.)

Prognosis and treatment: *Quoad vitam* the prognosis is favourable. Symptoms from the basilar impression are rare. The abnormal dental status needs special treatment. Possible concurrent rachitis may be considered to exacerbate the anomaly, and the rachitis should then be treated, of course.

These patients are generally discovered by chance, most likely because the anomaly gives no essential complaints. They may be found in different hospital wards and also by general practitioners—the chief thing is that one is observant of the condition.

SUMMARY

An account is given of a case of cleidocranial dysostosis with the typical deformities in the skull, the clavicles, the pelvis, and the hip joints.

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PAPILLOMA OF THE CHOROID PLEXUS WITH PULMONARY METASTASES

By

G. VRAA-JENSEN

Several reports have been published of gliomas, especially medulloblastomas, metastasizing into the subarachnoid space (cf. *Cairns & Russell* 1931), and subarachnoid dissemination of papillomas of the choroid plexus is not uncommon. Among 80 odd published case reports of papilloma of the choroid plexus *Herren*, in 1941, found secondaries in the cerebro-spinal fluid in no less than one fifth. As these tumours have their site in the ventricular system, it is not unnatural that they should spread in the subarachnoid space.

Subarachnoid dissemination from primary intracranial tumours, therefore, is not of uncommon occurrence, but extracranial metastases from primary brain tumours are extremely rare. Evidently, the conditions of growth in the central nervous system must be of quite a particular nature (cf. *Christensen, Kiær & Winblad* 1949). The extreme rarity of such metastases is apparent *inter alia* from a statement which according to *Bodechtel & Schüller* (1937) was made at a Pathologists' Congress in 1935: "Gliommetastasen in andere Körperorgane gibt es nicht, Liquormetastasen dagegen sind bei Gliomen ein relativ häufiges Ereignis." This statement does not, however, hold good. As early as 1936 *Nelson* published a case of cerebellar medulloblastoma with metastases in the bodies of the lowest thoracic vertebræ. Searching the literature of the preceding 10 years he found 7 additional cases of metastasizing intracranial tumours. Six of these growths had been examined histologically, but their nature could not be decided with certainty in all cases. *Nelson* also pointed out that there were a few older reports of distant metastases of intracranial tumours, but the latter were not sufficiently elucidated to be grouped in the present detailed classification of intracranial tumours.

Meningeal growths—mainly of a sarcomatous nature—appear to constitute the majority of metastasizing intracranial tumours. *Christensen, Kiær & Winblad* (1949) found 5 such cases in the literature and added 2 of their own. While preparing the present paper the writer was, however, unable to find any report of proven metastases of papilloma of the choroid plexus. *Deluén*, in 1936, published a small paper entitled “Métastase sur une vertèbre cervicale d'un néoplasme de la choroïde”. In this instance the nature and even the existence of the primary tumour as well as the supposed secondary lacked confirmation, and on the whole the diagnosis does not appear to be well-founded.

Below will be reported a case of papilloma of the choroid plexus running a malignant course which could be controlled histologically in connection with several operations and at the post-mortem examination, which revealed a cerebral metastasis as well as dissemination in both lungs of the same type as the brain tumour.

M.A. (Case rec. 974/48). A girl, born in August 1939. The patient entered the Copenhagen City Hospital, Department of Neurology in August 1946. During the last 2-3 months she had been complaining of attacks of headaches and now and then vomiting. These complaints increased, and gradually there was also diplopia and a sensation of pins and needles in the left arm.

Obj. exam.: Choking of the optic discs, right 4 D., left 2 D. Right-sided, partial paresis of the sixth nerve, mild paresis as well as marked ataxia and dysidiadokinesia of the left upper limb. Faint or absent reflexes of the upper limbs. Very slight spastic paresis of the left lower limb attended with exaggerated reflexes.

The patient was transferred to the University Hospital, Department of Neurosurgery, where operation revealed a partly cystic tumour of the right parietal lobe. The neoplastic tissue was granular and greyish red. The growth was removed *in toto* together with most of the oedematous glial tissue which surrounded it. The patient received post-operative X-ray therapy.

Histological examination of the operation specimen: The tumour contains a net of capillaries surrounded by one or more layers of radially disposed columnar cells with oblong nuclei and moderate chromatin. In the superficial parts of the tumour the papillomatous architecture is distinct. The structure of most of the tumour is blurred, but still shows the radial arrangement of the neoplastic cells around the blood-vessels, forming pseudo-rosettes in places. Mitotic figures are not demonstrable. Histological diagnosis: Papilloma of the choroid plexus, (sd. Erna Christensen).

Immediately after the operation the left-sided paresis was accentuated, but gradually it improved and the choking of the discs subsided in the course of a few months. The operation entailed a distinct personality change, the patient becoming more restless, talkative, forgetful, and on the whole more babyish than previously.

In June 1947 she was re-admitted to the Neuro-surgical Department, because 3 small, soft swellings had appeared in the scar. After ventriculography it was, however, decided to wait for some time before embarking on further interventions.

In October 1947 she came back, 15 months after the operation. In the course of the last 3 months the prominences at the site of the trephine holes had been steadily increasing in size. Objective examination revealed choked optic discs, right 3 D., left 2 D. Moderately severe spastic left-sided paresis with ataxia and left-sided astereognosis. At the posterior end of the scar there was a large, fluctuating prominence. Operation revealed a tumour consisting of a hemispherical extracranial formation with a diameter of about 5 cm. and a more irregular intracranial part measuring about 10 cm. in each direction. The tumour also involved the interjacent bone. The intracranial part of the tumour was in the right parietal lobe; it was partly cystic and occupied most of the lateral ventricle, sending an extension into the anterior as well as the descending horn. Subtotal excision of the tumour and removal of the portion of the dura above the tumour and the bone flaps.

Histological examination of the removed growth showed that it was richer in connective tissue than the tissue removed at the first operation. Moreover, it was more cellular and some of the cells were slightly atypical. Again, post-operative X-ray therapy was given; about a month after the operation the choking of the discs had almost subsided.

About 8 months after the second operation the patient was again admitted, as her condition had been deteriorating lately, and the site of the operation had been getting ever more tense. After a repeated course of X-radiation she was discharged, but shortly after—2½ years after the first operation—she had to be admitted to the Department of Neurosurgery where it was again attempted to remove the tumour which now projected like half a coco-nut from the site of the operation. In the course of this operation the tumour was found to be inoperable. The greater part was situated in the lateral ventricle, but a large portion was close to the falx. Since, moreover, the surrounding bone and the overlying skin were distinctly involved, only partial excision could be done.

Histological examination of the removed tissue showed mostly the same architecture as previously with the exception that now there were several polymorphous, atypical forms of cells, and numerous atypical processes of cell division were noted. Extensive necrotic areas were found in several places, particularly in the central portions. The boundaries between the tumour tissue and the surrounding cerebral tissue were ill-defined.

One week after the operation the patient was transferred to Kommunehospital, Department of Neurology, where she followed an even downhill course and died about 4 weeks after the operation.

Post-mortem examination showed a defect in the cranial wall overlying the right parietal region which was partly filled with cauliflower-like neoplastic tissue. On the surface of the brain there was a defect lined with tumour tissue in the right parietal lobe as well as a tumour of a type similar to the removed growth in the left occipital lobe. The latter growth, which measured about $6 \times 8 \times 10$ cm. and involved the cortex and part of the white matter, showed a somewhat irregular demarcation.

Numerous white, rather firm tumours, ½-1 cm. in diameter, were evenly distributed over both pleuræ. No pleural effusion. Tumours of the same nature and size were evenly distributed all over the lungs. Furthermore, both lower lobes exhibited moderate hyperæmia and atelectasis. No definite abnormalities in the hilar and bronchial lymph nodes. Otherwise, the post-mortem examination did not reveal anything abnormal, especially no tumours in other sites.

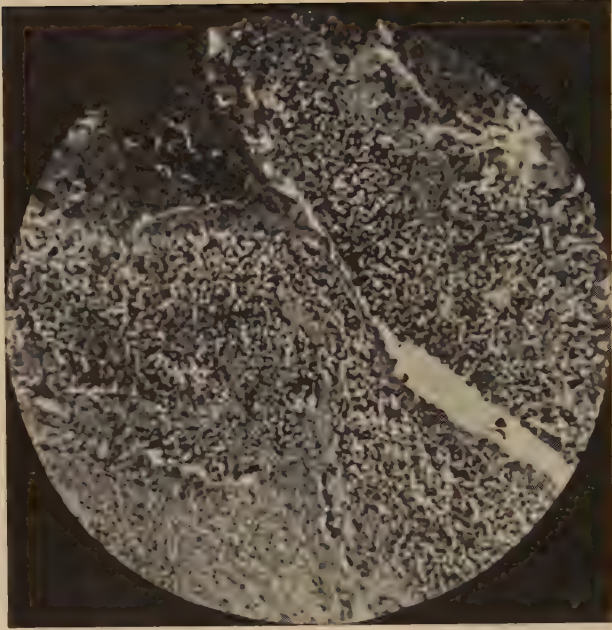


Fig. 1.
Primary tumour in the right parietal lobe. H.e. $\times 80$.

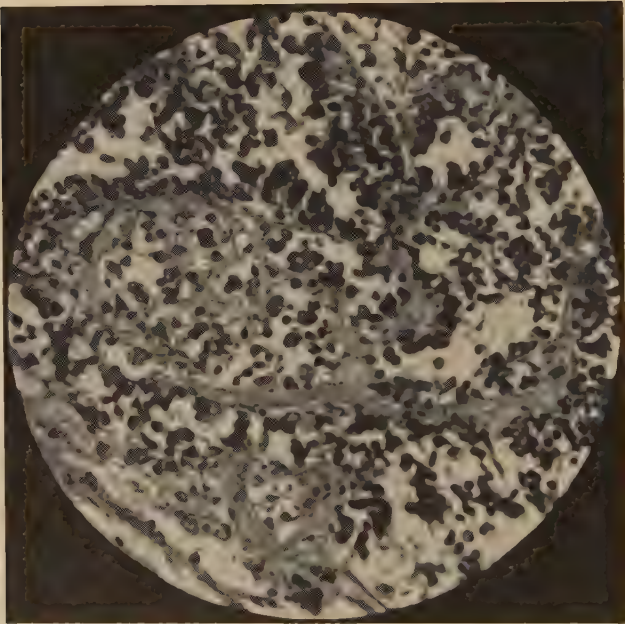


Fig. 2.
The same specimen. H.e. $\times 250$.

Histological examination. Sections from the site of the operation in the right parietal lobe showed in a few places tissue from the choroid plexus which failed to reveal anything abnormal. From these parts there was an even transition to typical tumour tissue. The appearance of the tumour was even more malignant than at the earlier examinations. It was made up of very thin strands of connective tissue beset with epithelium-like cells which varied in size, shape, and staining property. Most of the nuclei were oval to irregular, a few with several nucleoli. A few nuclei were pale, whereas others held ample chromatin. Several processes

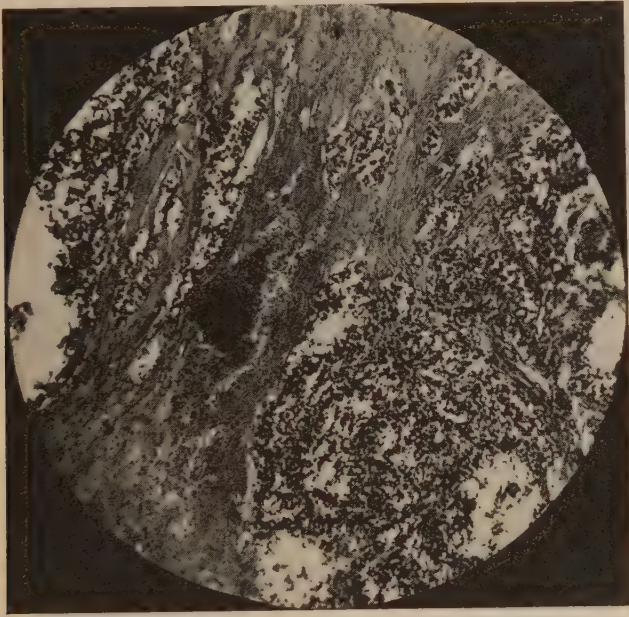


Fig. 3.

Section from the periphery of the trephine opening. H.e. $\times 80$.

of cell division were noted. In places the neoplastic tissue showed marked necrosis and extensive hæmorrhages, particularly in the central areas. The tumour was not everywhere sharply defined from the surrounding tissue. In the periphery of the growth the tissue was somewhat oedematous with ample proliferation of glial tissue and a number of major and minor blood-vessels many of which showed perivascular lymphocytic infiltration.

Sections from the periphery of the trephine opening showed that nearly everywhere the bony tissue was superseded by neoplastic tissue of an appearance identical with that just described. Only a few small, more or less structureless strands of bone remained in the tissue. The dura was also extensively involved in the neoplastic process.

Sections from the tumour of the occipital lobe also showed the structure described above; in this site, however, the limits towards the surrounding tissue were well-defined in the form of a thin connective-tissue membrane, in several places affected with lymphocytic infiltration. In the periphery the tissue was oedematous, showing several phagocytes. In the centre of the tumour there were

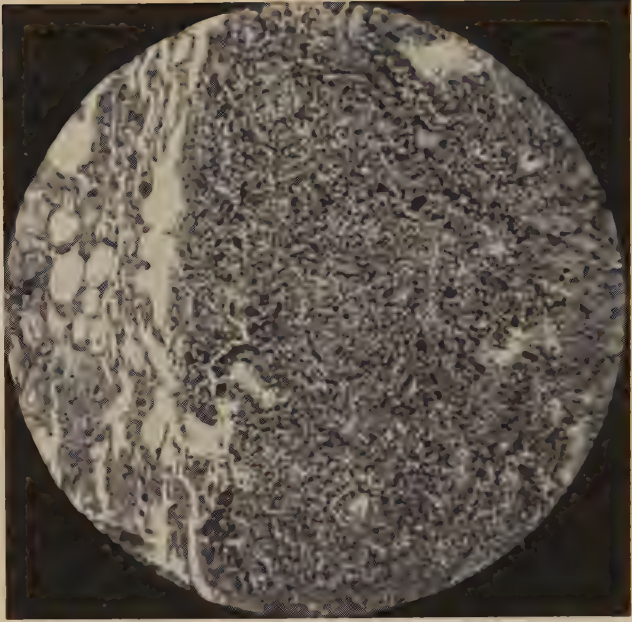


Fig. 4.
Section from a pulmonary metastasis. H. e. $\times 80$.

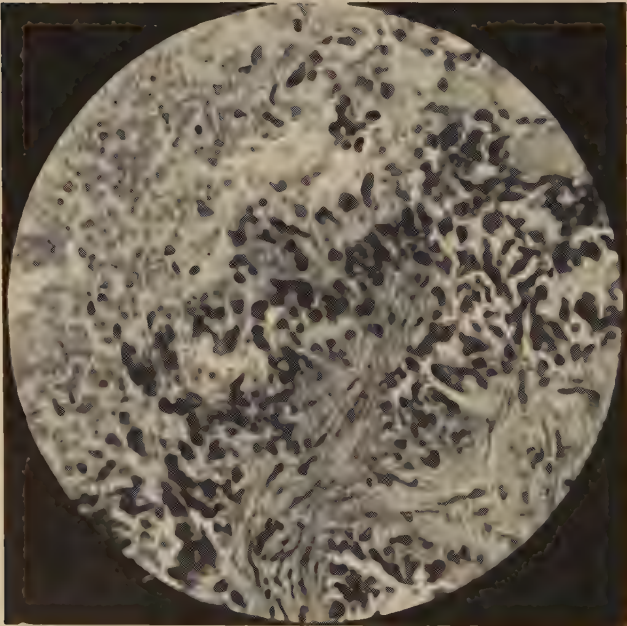


Fig. 5.
The same specimen. H. e. $\times 250$

a few major and minor areas filled with colloid and showing hæmorrhages in the margins.

Sections from the lung tumours were of exactly the same structure. Necrosis was noted in the largest growths, but not in the small ones. All the growths were circumscribed. In the periphery the pulmonary tissue was somewhat atelectatic and congested, in a few places showing mild inflammatory processes. Sections from the hilar and bronchial lymph nodes as well as from the mediastinum failed to exhibit neoplastic tissue.

COMMENT

In a comprehensive paper on primary carcinoma of the brain *Kufs* (1926) stated that he had never found convincing reports of primary carcinoma originating in the choroid plexus. Before this lesion could be diagnosed he demanded evidence of the unmistakable criteria of malignancy: destructive growth and metastases. These criteria were demonstrable in the case under discussion. The development of the tumour was followed histologically from the first apparently benign growth, through the ever more malignant recurrences exhibiting invasive growth as an increasingly outstanding feature, until the tumour post mortem showed: (1) distinct invasion of the surrounding brain tissue, dura, and bone, (2) extensive necroses and hæmorrhages, (3) marked atypia of the cells and numerous cell divisions. Moreover, there was (4) a typical intracranial metastasis connected with the subarachnoid space and sharply defined from the surrounding brain tissue by a thin connective tissue membrane. Regrettably, the spinal cord was not examined, and the writer is therefore unable to state whether the lesion had spread into the spinal subarachnoid space, a finding which has been reported by several workers (*Spiller* 1907, *Hall & Fentress* 1933, *Bodechtel & Schüler* 1937, and *Herren* 1941).

In addition, there was a phenomenon which has not been described before, i.e. (5) the lungs were sprinkled with numerous, circumscribed tumours which bore distinct marks of metastasization. The pulmonary metastases were of a structure exactly like the papilloma of the choroid plexus, and the post-mortem examination did not reveal other tumours which might account for the pulmonary metastases.

Beforehand it must be presumed that the metastasization was hæmatogenous, if it did arise from a brain tumour, and the situation of the secondaries in the lungs is also in favour of hæmatogenous dissemination.

SUMMARY

A girl, aged 7, was operated upon for a papilloma of the choroid plexus localized in the right parietal lobe. In the course of the subsequent $2\frac{1}{2}$ years she developed several recurrences of an ever more marked invasive growth and of a histological appearance suggesting increasing malignancy. Post-mortem examination revealed sub-arachnoid dissemination to the left occipital lobe as well as multiple metastases in both lungs and pleuræ. Histologically the metastases and the papilloma were of identical structure.

My thanks are due to Professor *E. Busch*, M.D., Department of Neurosurgery, Rigshospitalet, and *Sv. Petri*, M.D., pathologist to Kommunehospitalet, for permission to use the case records.

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ON RESPIRATION IN MELANCHOLIA

By

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Self-observation will convince everyone that variations in emotional balance affect the respiration. The sad breathe slowly and heavily, sighing deeply in between; the happy or expectant have a rapid and shallow respiration; the frightened, for a brief period, "forget" to breathe. The problem is: Do mental disorders of an elated or depressive nature, as found in mania and melancholia, affect respiration to a demonstrable degree?

Few reports have appeared of previous investigations into the question of respiration during the course of mental disorders. The first systematic investigations—made by *Sondén* (1927)—revealed, in eight patients with emotional disturbances, no changes in the rate of respiration that might definitely be ascribed to the mental changes ascertained. *Paterson*, in 1934, found that 121 schizophrenics breathed more shallowly and more rapidly than 62 normal subjects, whereas there were no definite deviations in respect of 25 melancholiacs. *Thompson, Corwin & Aste-Salazar* (1937 and 1942), in 25 schizophrenics, demonstrated considerably lower mean depths of respiration than in 25 normal subjects.

Golla, Mann & March (1928), and *March* (1929) have carried out the only previous experimental investigations with the object of determining the excitability of the respiratory centre in mental patients. They administered 2 per cent. carbon dioxide to the inspiratory air, and the latter report concludes with the observation that whereas 22 out of 25 (i.e. 88 per cent.) normal subjects reacted with increased ventilation of between 10 and 25 per cent., a similarly increased respiration was noted in only 6 out of 50 patients (suffering from schizophrenia, melancholia, mania, senile dementia, alcoholic dementia, or epilepsy)—i.e. 12 per cent.—while the rest of the patients presented insignificant increase or none at all. From a technical

point of view these experiments appear to be somewhat inadequate, and the material may be described as heterogenous, but, on the basis of their observations, the authors conclude that the excitability of the respiratory centre is reduced in mental diseases.

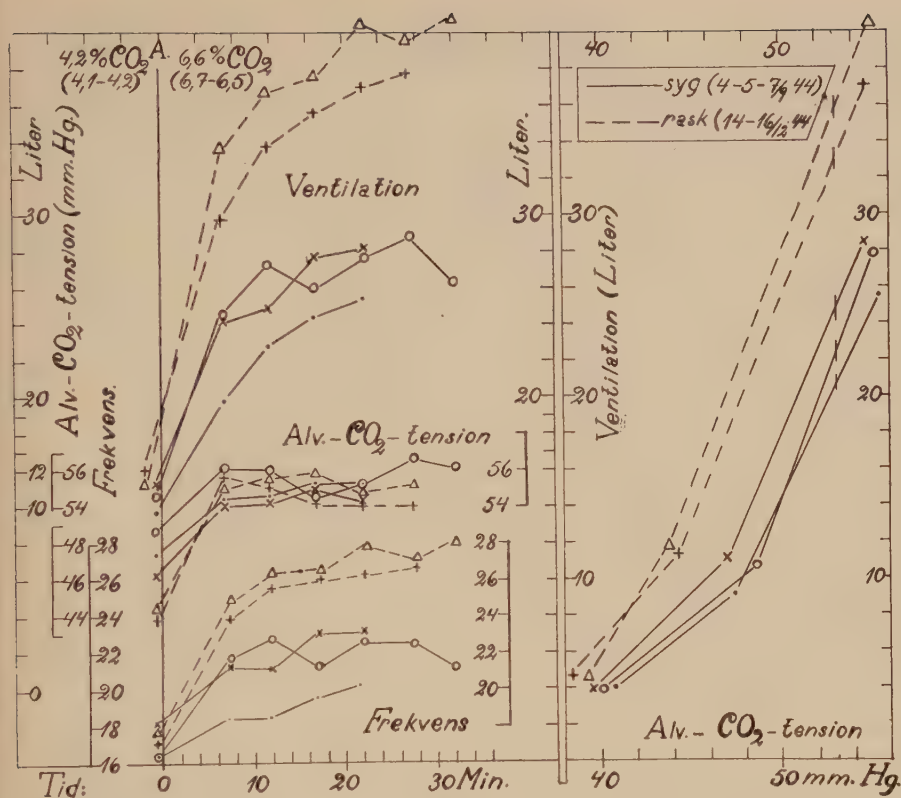
A more detailed and critical survey of previous investigations into the respiration in mental disorders is contained in my thesis "Undersøgelser over respirationscentrets følsomhed ved melankoli" (Investigations into the Excitability of the Respiratory Centre in Melancholia—in Danish: 1948).

That work comprises investigations into the respiration of 36 patients suffering from melancholia, carried out partly during the affection, and, partly, after recovery or improvement. The control material consists of 26 normal subjects.

The patients were all suffering from typical endogenous depressions, pronounced to a degree that justifies the designation of melancholia. The individual cases were regarded as types of *manic-depressive psychoses* or *periodic depressions*, or as *episodic onsets of melancholia*.—If the diagnosis "depressio mentis periodica" is not recognized as an independent diagnosis, all cases might without difficulty be referred to the manic-depressive complex of affections. Case reports are contained in my thesis.

Twenty-two of the patients recovered while in hospital, and the remaining 14 improved considerably. They were all examined from two to six (generally three) times in each period.

All examinations were carried out in the morning, and the subjects for examination were made to rest on a bed, fasting. Respiration took place through *Krogh's* valve (1923). After a rest period of at least half an hour, experiments were made with inspiration of atmospheric air followed by inspirations from Douglas bags of 4 and 6½ per cent. CO₂ in atmospheric air. The expired air was collected in a Douglas bag, which was emptied through a gas-meter after each experiment. The rate of respiration was determined, and ventilation and CO₂ in alveolar air was ascertained, the latter as directed by *Krogh & Lindhard* (1917) and by air analyses in a *Haldane-Krog* apparatus (*Lindhard*, 1927). Depth of respiration was computed, and the excitability of the respiratory centre was shown by an excitability curve, recorded by means of a graph, as directed by *Lindhard* (1911, 1933). For experimental details, errors, etc., see my above-mentioned thesis.—Definition of the conception *the excitability of the respiratory centre* is given by *Cohnstein & Zuntz* (1888) and *Lindhard* (1933).—In order to obtain a less complicated mode of expression I have (see my thesis, or report in the *Acta Physiologica Scandinavica* (19: 1949:



Figures 1-2.

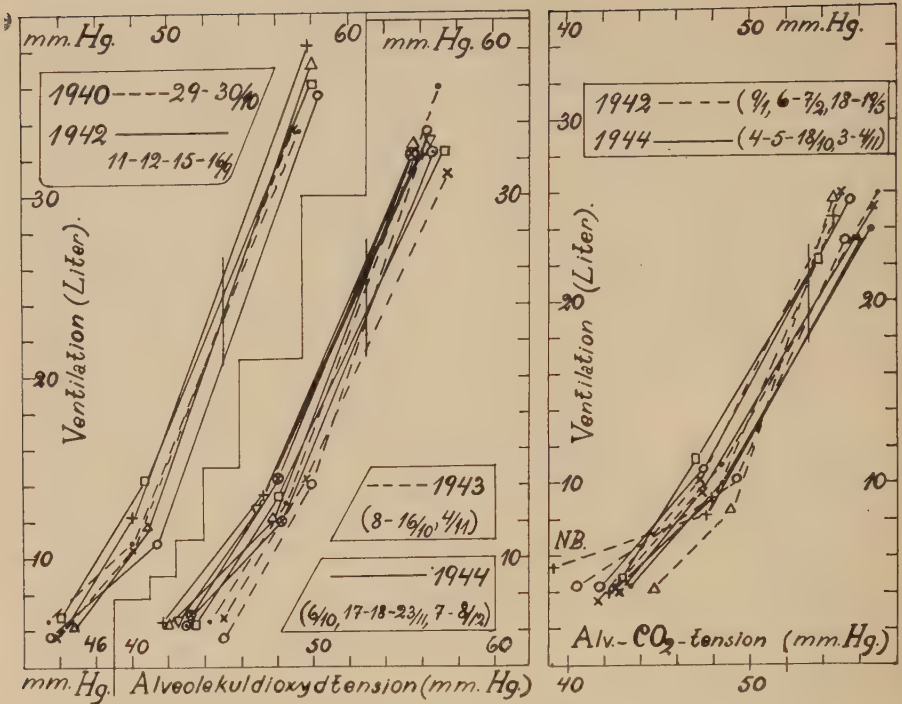
Experiments with patient.

Fig. 1: Ventilation, CO₂ tension in alveolar air, and rate in relation to time, as recorded from experiments with 4.2 % and 6.6 % CO₂ inspiration (figures of atmospheric air respiration not included for sake of clearness). At A the atmospheric air contents of CO₂ changes from 4.2 % to 6.6 %.—Ventilation at 6.6 % inspirations after recovery increases considerably when compared to melancholic period—the difference being about 13 litres per minute.—CO₂ tension in alveolar air shows no significant change, whereas the rate of respiration increases considerably on recovery.

Fig. 2: Excitability curves (according to Lindhard, 1933) showing considerable increase in the excitability of the respiratory centre upon recovery.

125)) designed a method according to which the excitability of the respiratory centre may be expressed by a figure—an excitability coefficient—based on Lindhard's excitability curves.

Of the 36 patients, 18 presented definitely, or considerably, reduced excitability of the respiratory centre during illness. A characteristic example is provided by Figs. 1-2. By way of comparison, Figs. 3-4 are taken from two normal subjects demonstrating no change in



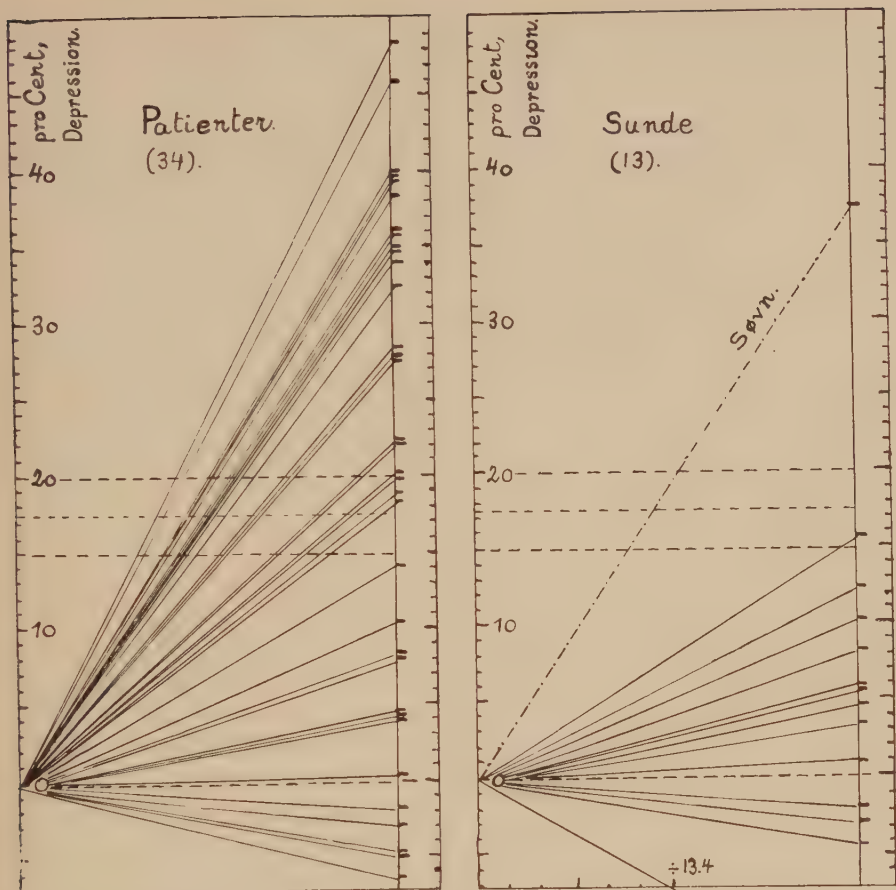
Figures 3 a and b, and 4.

Experiments with two healthy subjects, repeated through a number of years.

Figs. 3 a and b: Male, T.O., examined between 1940-1944. For comparison the experiments are collected in 2 + 2 groups.—The excitability of the respiratory centre almost constant; deviations very insignificant. Curves parallel, almost straight.

Fig. 4: Female, G.O., examined between 1942-1944. 1942 figures uncertain and varying with hyperventilation in atmospheric air experiments (NB). Gradually normal, almost straight curves. Changes in excitability of respiratory centre inconsiderable from year to year.

excitability at experiments at varying periods. Table 1 gives total results of experiments with the patients; it states (average) excitability coefficients during melancholia, as well as after recovery or improvement. Besides, possible reduction of excitability during illness is stated (in percentages). The maximum total reduction during melancholia appears to be 48.5 per cent. 22 patients reveal a reduction of upwards of 18 per cent. (average reduction 31.6 per cent.).—Table 2 shows the results of experiments with normal subjects. There are but slight differences at varying intervals. The greatest deviation is 15.8 per cent.—Table 3 gives average figures, and it may be noticed that the aggregate reduction of excitability in melancholia (17.6 per cent.)



Figures 5-6.

Differences—in percentages—between excitability coefficients ascertained at experiments during two periods, in patients and in normal subjects.

Fig. 5: 34 patients: reductions in excitability during melancholia; in percentages.

Fig. 6: 13 normal subjects: variations in excitability ascertained during two periods; in percentages. Dot-and-dash line shows (in percentages) average reduction of excitability during sleep; the result is obtained through ten experiments on two subjects.

exceeds the maximum reduction in normals (15.8 per cent.) The average deviation in normal subjects was 6.4 per cent.

Figures 5-6 give a graphic presentation, in percentages, of reduction of excitability during melancholia as compared with the variations, in percentages, in normal subjects. The difference is obvious.

Fig. 6, besides, shows the average reduction of the excitability of the respiratory centre during sleep, recorded from a total of ten experiments. The reduction of excitability in melancholia thus

appears to be of the same magnitude as the physiological reduction during sleep. With regard to these experiments during sleep, see my thesis.

It appears from Table 4 that the patients in whom the excitability of the respiratory centre was reduced during melancholia, also present changes in rate and depth of respiration and of ventilation. The ventilation increases by up to 13.7 litres per minute by $6\frac{1}{2}$ per cent. CO_2 inspiration, and, after recovery or improvement, by up to 2.1 litres by inspiration of atmospheric air. Inspirations of $6\frac{1}{2}$ per cent. CO_2 after recovery in all cases show increased rate of respiration, up to 25 per cent. Experiments with respiration in atmospheric air yield slightly more irregular results caused by a tendency to hyperventilation in these cases as compared with CO_2 inspiration by inexperienced subjects. Table 5 lists the results of experiments with the remaining 18 patients in whom the excitability of the respiratory centre underwent no definite or typical change by recovery; and Table 6 shows the conditions in normal subjects. These two groups present the same general picture: small, irregular deviations from one period to the other, now a slight rise, now a slight fall in the results obtained. By computation of average figures (see Table 9) these differences will counterbalance each other. The first two trained experimental subjects presented very insignificant variations from year to year. Finally, determinations at various periods of the CO_2 tension in the alveolar air of patients and normal subjects have been collected in Tables 7 and 8. In cases of reduced excitability during melancholia the tension was found to be constantly and correspondingly increased, differences between the two periods generally being 2 to 3 mm.Hg. Also in these cases, however, slight inaccuracies may attach to the atmospheric inspiration figures.

As will be seen from the above-mentioned tables, the individual variations—in excitability of the respiratory centre as well as in rate and depth of respiration, in ventilation, and in alveolar CO_2 tension—in affected and in healthy persons—are very pronounced. (With regard to this point see the report in the *Acta Physiologica Scandinavica* 1949—"The Individual Variability in Respiration").

Table 9 gives average figures which show a mean reduction of ventilation of 0.5 litres at atmospheric respiration during melancholia, whereas the reduction during $6\frac{1}{2}$ per cent. CO_2 inspirations averages 6.9 litres. Rate and depth fall accordingly, and alveolar CO_2 tension increases by 1.2 and 2.3 mm., respectively. The remaining patients present no essential changes. Average figures for all patients reveal some reduction of ventilation (0.4 and 3.6 litres), rate (0.1 and 1.3),

and depth (25 to 110 ccm), as well as some increase of alveolar CO₂ tension (0.8 and 0.7 mm.Hg.). There is no difference in the figures obtained at various periods in normal subjects (Table 10).

Special investigations with the object of revealing factors that might affect the results of the experiments—loss of weight, experience in respiration tests, length of rest periods before experiments, confinement to bed, lack of sleep, menstruation, seasonal variations, shock treatment, special symptoms as such psychic inhibitions, etc.—have failed to demonstrate other causes of reduced excitability than the state of melancholia.

This writer has not succeeded in explaining the reason why only half of the patients examined have shown reduced excitability of the respiratory centre during melancholia.—The reduction of excitability is therefore most likely to be regarded as a symptom of that affection, frequently, but not always, present.

7.

SUMMARY

Out of 36 patients suffering from melancholia, 18 presented pronounced reduction of the excitability of the respiratory centre during the disease, whereas the remaining patients showed no definite or typical change of excitability. Further, in the former group was ascertained decreased ventilation, rate and depth of respiration, as well as increased CO₂ tension in the alveolar air.

Experiments with 26 normal subjects revealed no respiratory changes when the subjects were examined at varying intervals.

The individual variability in respiration was found to be considerable.

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TABLE 1

Pt. No.	State	E. C.	Reduct.	Pt. No.	State	E. C.	Reduct.
1.	sick	22.4	35.0	12.	sick	11.7	18.4
	recovered	34.4			recovered	14.7	
2.	sick	16.0	32.5	30.	sick	9.5	22.4
	recovered	23.7			improved	12.2	
3.	sick	11.2	48.5	31.	sick	11.5	22.3
	recovered	21.7			improved	14.8	
4.	sick	15.2	27.6	13a.	sick	19.8	(3.8)
	recovered	21.0			recovered	18.6	
5.	sick	13.4	19.8	13b.	sick	19.0	(4.2)
	recovered	16.7			recovered	18.2	
6.	sick	11.1	36.2	14.	sick	24.2	4.0
	recovered	17.4			recovered	25.2	
7.	sick	17.1	39.5	15.	sick	26.6	(4.7)
	recovered	28.5			recovered	25.4	
8a.	sick	9.9	37.5	16.	sick	22.2	6.3
	recovered	15.8			recovered	23.7	
8b.	sick	9.0	38.8	17.	sick	19.6	(4.7)
	recovered	14.7			recovered	18.7	
9.	sick	20.2	20.2	18.	sick	19.5	4.0
	recovered	25.3			recovered	20.5	
10.	sick	12.2	28.4	19.	sick	17.1	(1.8)
	recovered	18.7			recovered	16.8	
11.	sick	21.0	18.8	20.	sick	19.7	8.0
	recovered	26.0			recovered	21.4	
23.	sick	13.2	46.0	21.	sick	18.8	4.1
	improved	24.4			recovered	19.6	
24.	sick	10.7	40.0	32.	sick	24.5	(2.8)
	improved	17.8			improved	24.0	
25.	sick	9.7	39.8	33.	sick	17.2	10.4
	improved	16.1			improved	19.2	
26.	sick	11.3	34.0	34.	sick	14.7	0.0
	improved	15.6			improved	14.7	
27.	sick	10.6	36.0	35.	sick	22.0	(6.3)
	improved	15.0			improved	20.7	
28.	sick	18.1	27.9	22.	sick	8.9	32.0
	improved	25.1			recovered	13.1	
29.	sick	15.7	34.8	36.	sick	25.0	(29.0)
	improved	24.1			improved	19.4	

Excitability coefficients for all 36 patients, expressed by figures representing average experimental results during periods of sickness and health (or improved health). Figures to the right of the coefficients give the reduction (or, when in brackets, the increase) of excitability during melancholia, reckoned in percentages of the results obtained during recovery or improvement.

E. C.: Excitability coefficient.

Reduct.: Reduction of excitability during melancholia, in percentages.

TABLE 2

Subject	Time	E.D.	Var	Subject	Time	E.D.	Var
G.L.	1945	31.7	5.9	G.A.	1943	29.0	1.0
	1945	33.7			1944	29.3	
T.Ø.	1940	23.2	6.1	H.H.	1943	43.0	(12.8)
	1942	23.4	5.3		1944	43.3	(13.4)
	1943	23.2	6.1		1945	37.5	
	1944	24.7		C.T.	1940	37.7	15.8
G.Ø.	1942	20.3	(4.5)		1942	44.8	
	1944	19.4		M.S.	1943	36.0	
R.F.	1943	21.4	(3.3)	B.S.	1942	27.5	
	1944	19.4		M.H.	1942	31.2	
T.B.	1944	16.6	(1.8)	E.L.	1942	25.0	
	1945	16.3		H.B.	1940	22.4	
K.K.	1943	11.1	8.3	E.B.	1942	23.3	
	1944	12.1		G.S.	1940	18.2	
G.P.	1940	19.6	(2.6)	T.T.	1942	35.7	
	1943	19.1		T.F.	1942	32.5	
E.A.	1943	17.4	12.3	A.B.	1942	27.2	
	1944	19.9		A.A.	1942	27.5	
E.E.	1943	18.3	6.2	W.S.	1940	23.7	
	1944	18.9	3.1	O.K.	1942	13.0	
	1945	19.5					
H.W.	1943	20.5	10.1				
	1944	22.8					

Table of excitability coefficients obtained from experiments with 26 normal subjects; 13 of these were examined during two, and 13 during one, period(s). Figures represent average results of all experiments within each period.

E.C.: Excitability coefficient.

Var.: Variation in excitability when comparing the two periods.

TABLE 3

Patients		E.C.	Reduct. %
Total number (36)	during sickness	16.6	17.6
	when recovered or improved	20.2	
Changed excitability (in 18)	during sickness	14.7	31.6
	when recovered or improved	21.5	
<i>Normal Subjects</i>			
Total number (26)		25.2	

Average excitability coefficients (E.C.) for all patients during the two periods and for all normal subjects; besides, average reduction of excitability, in percentages (Reduct. %).

TABLE 5

Pt. No.	State	Atmosph. respiration			4 % CO ₂ respiration			6 1/2 % CO ₂ respiration		
		V.	R.	D.	V.	R.	D.	V.	R.	D.
13a.	sick	5.8	20.1	290	13.1	21.2	615	24.7	21.6	1150
	recovered	6.1	24.4	250	13.1	23.5	555	25.8	22.3	1155
13b.	sick	5.6	16.9	330	12.3	16.8	735	25.4	20.8	1240
	recovered	5.3	14.4	355	12.1	15.8	770	16.2	21.2	1240
13c.	sick	4.9	13.9	395	11.3	16.3	695	25.9	20.1	1290
	recovered	5.1	14.3	360	11.7	16.1	725	26.8	21.3	1260
14°).	sick	6.2	14.9	415	12.4	18.1	680	31.0	21.7	1430
	recovered	5.9	14.7	400	11.9	18.0	665	31.3	21.0	1495
15°).	sick	7.2	17.1	420	15.6	17.2	910	28.9	16.7	1740
	recovered	9.0	22.1	410	15.1	18.4	820	26.8	16.2	1660
16°).	sick	7.2	20.6	350	12.9	21.3	615	23.8	22.3	1080
	recovered	6.9	18.8	370	13.0	19.0	685	22.5	20.5	1100
17.	sick	4.4	10.8	405	9.4	12.4	760	22.2	16.1	1380
	recovered	4.6	11.6	400	8.4	12.0	700	22.5	16.2	1390
18.	sick	9.3	27.6	345	12.4	26.4	470	23.1	23.0	1010
	recovered	8.8	23.2	380	14.2	21.7	585	26.3	24.9	1105
19.	sick	5.3	18.3	290	10.1	21.2	480	19.2	22.1	870
	recovered	4.8	18.1	265	10.5	20.6	510	20.1	22.7	890
20.	sick	4.8	16.9	285	10.0	19.8	505	20.9	22.2	940
	recovered	4.8	17.8	270	11.5	20.3	520	22.8	22.9	995
21.	sick	4.3	13.4	320	9.5	17.4	535	21.2	20.0	1060
	recovered	4.5	12.7	355	9.6	16.6	575	19.9	18.3	1085
32.	sick	5.7	13.2	435	11.3	17.0	665	27.7	23.1	1200
	improved	6.0	13.4	445	11.7	17.4	670	27.3	22.0	1240
33.	sick	5.4	12.3	440	9.4	13.0	725	22.6	15.8	1435
	improved	5.1	12.0	425	10.4	13.4	715	24.7	17.2	1435
34.	sick	5.7	22.0	260	11.8	23.0	510	19.0	22.3	855
	improved	5.7	23.2	245	11.2	24.7	450	21.4	23.0	930
35.	sick	6.8	11.0	620	9.4	12.5	750	24.2	18.6	1320
	improved	7.4	11.6	640	10.3	13.3	780	23.5	19.0	1240
12.	sick	3.8	15.8	240	9.3	16.6	555	16.6	18.2	915
	recovered	4.2	16.8	250	9.7	16.9	585	20.3	19.5	1050
30.	sick	4.5	12.3	365	8.1	13.6	595	14.3	15.5	925
	improved	4.1	11.5	360	8.4	13.1	640	17.4	17.1	1020
31.	sick	3.9	14.9	260	7.3	16.2	450	15.0	18.3	820
	improved	4.3	13.9	310	8.0	14.4	555	17.5	20.0	875
22.	sick	4.0	10.3	395	8.6	14.7	585	18.8	17.6	1070
	recovered	5.1	12.8	400	9.9	13.4	740	19.2	16.5	1060
36.	sick	5.1	13.4	380	10.5	15.0	700	34.7	20.9	1660
	improved	6.1	12.7	475	11.0	12.5	880	33.1	19.7	1690

18 patients, presenting no definite reduction of excitability of the respiratory centre during melancholia: average ventilation, rate and depth of respiration ascertained at two periods, during affection and after recovery or improvement. Patients marked °) are males. Patient No. 13 was examined during three periods of melancholia (a, b, and c).

V.: Ventilation in litres per minute.

R.: Rate of respiration per minute.

D.: Depth of respiration in ccm.

TABLE 4

Pt. No.	State	Atmosph. respiration			4 % CO ₂ respiration			6½ % CO ₂ respiration.		
		V.	R.	D.	V.	R.	D.	V.	R.	D.
1.	recovered	4.4	13.3	330	10.3	17.5	590	27.5	22.5	1220
	sick	4.4	13.2	330	12.5	17.5	710	39.7	30.5	1300
2°).	sick	7.3	13.4	585	12.2	16.4	745	28.3	22.0	1280
3.	recovered	8.0	10.0	800	11.4	13.0	880	39.0	23.2	1680
	sick	4.5	13.0	345	7.5	14.6	515	18.9	18.8	1005
4.	recovered	5.5	14.9	370	10.5	16.7	630	29.2	22.6	1320
	sick	4.7	14.1	335	9.6	13.8	695	20.0	19.1	1050
5.	recovered	5.7	15.3	360	11.5	16.1	715	29.9	23.9	1250
	sick	5.2	11.1	470	10.1	12.5	805	17.8	13.4	1330
6.	recovered	4.8	9.8	490	10.2	11.3	905	21.4	12.3	1740
	sick	3.5	5.0	605	7.9	7.4	1070	17.0	10.1	1690
7.	recovered	3.9	8.2	480	10.8	9.9	1090	24.3	14.0	1740
	sick	5.3	17.3	310	10.0	16.9	590	20.8	20.9	970
8a.	recovered	6.0	19.2	310	12.6	21.2	590	27.8	25.5	1070
	sick	4.3	16.2	265	7.8	15.6	500	16.9	16.9	1000
8b.	recovered	5.0	16.9	300	9.4	16.7	560	20.5	20.0	1030
	sick	4.0	13.7	290	7.9	15.2	520	16.2	16.0	1010
9°).	recovered	4.5	13.8	330	9.9	21.0	650	20.0	18.0	1110
	sick	7.6	23.3	325	12.1	22.2	545	27.9	20.9	1340
10.	recovered	7.8	19.8	395	13.7	21.0	650	32.4	23.6	1380
	sick	4.4	18.0	230	8.6	18.0	540	15.5	19.3	840
11.	recovered	4.7	15.5	300	10.6	18.8	565	20.4	20.0	1020
	sick	5.8	14.8	390	13.7	16.1	850	28.1	22.8	1230
23.	recovered	5.9	15.3	390	15.8	18.6	850	28.9	22.6	1280
	sick	4.2	18.8	225	7.8	18.6	420	18.4	18.2	1010
24°).	improved	6.3	16.0	395	11.9	18.5	615	31.7	23.7	1340
	sick	5.9	12.2	485	10.7	13.2	810	21.2	16.2	1310
25.	improved	5.8	12.6	460	12.4	14.6	850	29.1	17.6	1650
	sick	3.7	10.2	360	7.9	13.6	580	18.3	16.9	1080
26.	improved	4.0	11.4	350	9.9	13.0	760	20.7	16.1	1290
	sick	5.1	19.8	265	8.5	20.3	425	13.9	21.7	635
27.	improved	6.2	19.9	310	9.8	20.5	480	19.0	21.0	910
	sick	4.4	12.2	360	7.3	14.3	510	15.1	15.1	1000
28.	improved	4.4	12.6	350	9.9	16.3	610	19.9	16.7	1190
	sick	4.5	12.6	360	9.2	15.1	610	20.8	18.8	1100
29.	improved	6.4	15.5	410	9.5	16.6	570	30.6	22.2	1380
	sick	5.3	15.6	340	9.8	15.8	620	22.6	18.3	1240
	improved	5.2	17.1	305	13.0	16.7	780	29.2	20.4	1430

18 patients, presenting reduced excitability of the respiratory centre during melancholia: average ventilation, rate and depth of respiration ascertained at two periods, during affection and after recovery or improvement. Patients marked °) are males.

Patient No. 8 was examined during two periods of melancholia (a and b).

V.: Ventilation in litres per minute.

R.: Rate of respiration per minute.

D.: Depth of respiration in ccm.

TABLE 6

Subj.	Time	Atmosph. respiration			4 % CO ₂ respiration			6½ % CO ₂ respiration		
		V.	R.	D.	V.	R.	D.	V.	R.	D.
T.Ø.°)	1940	6.1	14.9	410	10.7	16.6	645	33.7	22.3	1510
	1942	6.2	14.8	420	12.3	17.5	700	36.3	22.3	1650
	1943	6.3	16.0	395	13.6	17.1	790	36.5	21.6	1690
	1944	6.3	15.1	415	13.2	16.7	790	35.4	21.7	1640
G.Ø.	1942	4.4	14.8	300	9.8	15.9	615	25.0	19.6	1270
	1944	4.3	13.0	330	10.2	16.1	635	23.3	20.3	1180
	1945	4.9	14.2	345	10.2	16.8	610	21.1	24.0	1130
E.E.	1943	5.0	16.8	300	12.6	17.7	710	25.3	21.2	1200
	1944	5.0	16.2	310	12.7	17.7	715	25.8	20.4	1260
	1945	4.4	13.2	330	13.6	17.1	795	25.8	19.5	1320
H.H.	1943	6.6	11.1	595	13.0	12.5	1040	52.4	28.0	1850
	1944	4.7	10.7	460	16.2	13.3	1220	50.0	27.0	1850
	1945	4.4	8.4	525	14.1	11.6	1215	43.5	23.5	1850
G.L.	1945	5.6	14.5	385	16.8	19.0	885	39.0	23.5	1660
	1945	5.3	15.7	340	17.7	20.4	865	39.0	22.0	1770
R.F.	1943	4.3	7.5	570	10.2	10.8	950	24.7	16.2	1530
	1944	4.0	7.6	525	9.0	10.0	900	26.7	17.2	1550
T.B.	1943	4.4	12.0	370	9.2	13.9	660	25.0	18.0	1390
	1945	4.4	11.2	390	9.4	13.3	705	24.8	17.8	1390
K.K.	1943	4.3	9.3	460	9.1	9.2	990	20.3	13.7	1400
	1944	5.0	10.0	500	9.1	9.9	920	19.4	13.6	1430
G.P.	1940	4.9	18.9	260	11.0	20.5	535	22.0	21.4	1030
	1943	4.7	17.1	275	12.3	20.1	610	25.6	23.7	1080
E.A.	1943	4.8	12.5	385	10.5	13.3	790	25.3	19.8	1280
	1943	4.7	12.7	370	10.9	12.8	850	26.0	19.2	1360
H.W.	1943	5.5	12.8	430	11.7	13.9	840	30.5	20.2	1510
	1944	5.3	12.0	440	11.4	15.1	760	32.2	20.0	1610
G.A.	1943	5.9	10.0	590	13.0	12.4	1050	36.8	26.5	1390
	1944	6.1	12.0	510	14.0	14.6	960	36.5	26.8	1360
C.T.°)	1940	6.3	16.5	380	11.7	16.5	710	47.5	25.3	1880
	1942	5.4	14.0	385	12.2	15.4	790	46.9	25.7	1820
M.S.	1943	7.5	22.0	340	17.8	21.5	825	41.5	34.8	1190
B.S.	1942	5.2	15.5	335	14.9	16.0	930	33.8	20.9	1620
M.H.	1942	6.0	20.0	300	16.6	19.2	865	31.3	27.0	1150
E.L.	1942	4.7	9.8	480	11.3	13.0	885	30.7	23.5	1310
H.B.	1940	5.4	16.6	325	10.4	20.1	515	25.4	37.5	680
E.B.	1942	4.7	13.5	350	13.5	15.5	870	24.8	19.0	1305
G.S.	1940	5.1	19.5	260	10.0	20.1	495	20.2	23.1	875
T.T.°)	1942	6.8	14.9	465	17.6	18.8	930	40.1	28.0	1440
T.F.°)	1942	6.4	15.0	440	12.4	16.5	750	39.7	25.2	1580
A.B.°)	1942	6.6	12.4	535	12.9	14.0	920	36.0	20.4	1770
A.A.°)	1942	5.1	11.9	430	11.9	13.0	920	32.1	19.3	1670
W.S.°)	1940	5.7	15.5	370	11.7	16.9	690	26.7	18.7	1430
O.K.°)	1942	5.1	10.9	470	10.8	16.9	640	25.2	21.9	1150

26 normal subjects, examined during one or more periods: average ventilation, rate and depth of respiration. Subjects marked °) are males.

V.: Ventilation in litres per minute.

R.: Rate of respiration per minute.

D.: Depth of respiration in ccm.

TABLE 7

Pt. No.	State	Atmosph. 4 % CO ₂ 6½ % CO ₂			Pt. No.	State	Atmosph. 4 % CO ₂ 6½ % CO ₂		
1.	sick	39.2	46.7	55.7	13a.	sick	38.4	45.6	55.5
	recovered	38.7	43.8	54.9		recovered	37.1	45.8	57.1
2°).	sick	40.5	51.3	59.5	13b.	sick	42.8	48.6	57.1
	recovered	36.5	48.7	59.1		recovered	40.0	49.3	57.4
3.	sick	43.0	50.8	57.6	13c.	sick	41.6	46.9	57.3
	recovered	41.6	47.5	57.0		recovered	40.8	46.7	56.7
4.	sick	40.6	47.6	57.3	14°).	sick	42.4	47.2	55.9
	recovered	39.2	46.3	56.4		recovered	40.8	46.5	55.6
5.	sick	44.6	49.6	57.3	15°).	sick	36.5	44.9	56.1
	recovered	39.3	46.9	57.2		recovered	31.6	43.8	57.2
6.	sick	44.9	49.5	60.0	16°).	sick	38.2	44.2	55.1
	recovered	42.1	48.8	58.2		recovered	35.6	43.9	54.4
7.	sick	40.1	48.4	55.2	17.	sick	38.5	44.1	56.0
	recovered	37.1	45.8	52.8		recovered	38.5	44.7	56.3
8a.	sick	42.6	51.7	61.9	18.	sick	36.2	44.6	56.5
	recovered	38.8	47.0	56.7		recovered	35.8	45.8	54.9
8b.	sick	43.1	51.7	60.4	19.	sick	37.6	43.6	54.1
	recovered	41.4	48.3	57.8		recovered	38.4	45.1	56.8
9°).	sick	40.4	48.0	57.2	20.	sick	37.4	42.8	53.9
	recovered	38.2	46.9	56.6		recovered	39.8	44.1	54.1
10.	sick	39.2	46.7	56.4	21.	sick	38.7	44.5	54.7
	recovered	39.0	45.4	54.7		recovered	38.0	45.0	54.4
11.	sick	35.8	64.4	58.5	32.	sick	37.8	44.5	55.6
	recovered	33.7	44.3	55.0		improved	35.0	44.3	55.7
23.	sick	36.0	46.6	58.9	33.	sick	40.9	47.1	57.0
	improved	35.8	45.1	57.9		improved	39.8	46.3	56.4
24°).	sick	46.7	53.0	59.9	34.	sick	35.5	48.1	60.0
	improved	43.0	49.4	59.9		improved	35.1	47.1	60.0
25.	sick	45.0	51.7	57.9	35.	sick	31.3	43.9	56.3
	improved	41.9	48.6	56.5		improved	30.8	44.8	56.6
26.	sick	39.7	48.2	58.1	12.	sick	42.8	50.5	58.6
	improved	39.6	45.8	57.9		improved	40.8	49.3	58.0
27.	sick	42.7	49.9	57.1	30.	sick	42.4	49.5	59.8
	improved	40.2	47.3	55.8		improved	41.4	49.1	58.9
28.	sick	40.5	46.6	55.9	31.	sick	38.0	47.8	56.9
	improved	35.2	44.2	55.9		improved	37.4	46.7	56.1
29.	sick	38.0	47.3	57.8	22.	sick	45.9	52.6	59.5
	improved	37.8	45.7	56.1		recovered	42.3	49.0	59.5
					36.	sick	40.5	47.2	57.0
						improved	41.7	49.6	58.9

Experiments with patients during melancholia and after recovery or improvement: average CO₂ tension in alveolar air (mm. Hg.). Left-hand column: patients with reduced excitability of respiratory centre during melancholia. Right-hand column: patients with no or uncertain reduction.—Patients Nos. 8 and 13 were examined during several periods of melancholia.—Patients marked °) are males.

TABLE 8

Subj.	Time	Atmosph. 4 % CO ₂	6 ¹ / ₂ % CO ₂	Subj.	Time	Atmosph. 4 % CO ₂	6 ¹ / ₂ % CO ₂
T.Ø.°)	1940	43.8	48.0	57.1	E.A.	1943	42.1 48.8 57.5
	1942	44.0	48.8	58.0		1943	40.2 47.2 56.8
	1943	44.6	49.0	57.6	H.W.	1943	41.3 48.8 57.1
	1944	42.9	47.8	56.2		1944	40.9 47.7 57.1
G.Ø.	1942	42.3	48.3	55.3	G.A.	1943	38.6 46.1 56.3
	1944	42.7	47.8	55.6		1944	38.0 45.0 56.2
	1945	42.8	49.2	56.2	C.T.°)	1940	40.2 45.9 55.6
E.E.	1943	40.2	50.3	56.8		1942	40.6 44.6 56.2
	1944	40.5	49.5	57.0	M.S.	1943	35.2 44.0 55.7
	1945	39.0	48.6	56.4	B.S.	1942	37.8 45.7 55.9
H.H.	1943	36.8	44.2	55.7	M.H.	1942	35.8 43.7 52.7
	1944	39.0	45.7	54.7	E.L.	1942	39.0 44.8 56.3
	1945	40.6	45.9	55.3	H.B.	1940	40.0 46.1 55.2
G.L.	1945	36.1	46.7	56.6	E.B.	1942	37.8 46.9 54.0
	1945	35.9	46.1	55.2	G.S.	1940	40.7 47.0 54.2
R.F.	1943	39.8	45.6	55.2	T.T.°)	1942	39.4 47.3 54.1
	1944	40.9	46.3	56.3	T.F.°)	1942	40.3 47.1 55.2
T.B.	1943	42.8	49.8	57.1	A.B.°)	1942	41.8 46.4 57.2
	1945	43.1	49.4	57.6	A.A.°)	1942	42.2 47.7 54.1
K.K.	1943	43.8	51.2	59.8	W.S.°)	1940	41.5 46.5 54.4
	1944	39.9	48.8	58.6	O.K.°)	1942	47.5 52.0 59.5
G.P.	1940	40.2	45.8	54.8			
	1943	39.9	47.0	58.0			

All experiments with normal subjects: average CO₂ tension in alveolar air (mm. Hg.). The first 13 subjects were examined during two or more periods, the remaining 13 during one period only. The two first are trained subjects. Subjects marked °) are males.

TABLE 9

Patients	Atmospheric respiration				4 % CO ₂ respiration				6 1/2 % CO ₂ respiration			
	V.	R.	D.	A.	V.	R.	D.	A.	V.	R.	D.	A.
Changed (18):												
Sick	5.0	14.5	350	41.1	9.5	15.6	610	48.9	20.5	18.4	1115	57.8
Recvd. or impr.	5.5	14.6	380	38.8	11.5	16.4	690	46.6	27.4	20.8	1320	56.6
Unchanged (16):												
Sick	5.6	16.2	345	38.4	10.8	17.7	610	45.9	22.5	19.9	1110	56.5
Recvd. or impr.	5.7	16.2	350	37.3	11.0	17.6	625	45.9	22.9	20.3	1120	56.4
Total (36):												
Sick	5.2	15.1	345	39.2	10.1	16.5	610	47.5	21.6	19.1	1130	57.2
Recvd. or impr.	5.6	15.2	370	38.4	11.1	16.7	665	46.4	25.2	20.4	1240	56.5

Experiments with all patients: average ventilation, rate and depth of respiration, and CO₂ tension in alveolar air. Results from the two phases (sickness, and recovery or improvement) have been calculated separately and tabulated for comparison.

V.: Ventilation in litres per minute.

R.: Rate of respiration per minute.

D.: Depth of respiration in ccm.

A.: CO₂ tension in alveolar air (mm. Hg.).

TABLE 10

Normal Subjects	Atmospheric respiration				4 % CO ₂ respiration				6 1/2 % CO ₂ respiration			
	V.	R.	D.	A.	V.	R.	D.	A.	V.	R.	D.	A.
Examined during two periods (13):												
1st period:	5.2	13.2	395	40.6	12.0	14.8	810	47.7	31.3	21.2	1480	56.5
2nd period:	5.0	12.6	395	40.0	12.1	14.9	810	47.2	31.0	21.1	1470	56.6
Average of												
total (26):	5.4	14.1	385	40.2	12.6	16.0	785	47.0	31.4	22.7	1380	5.60

Average ventilation, rate and depth of respiration and CO₂ tension in alveolar air in normal subjects, partly 13 examined during two periods, partly all 26 examined.

V.: Ventilation in litres per minute.

R.: Rate of respiration per minute.

D.: Depth of respiration in ccm.

A.: CO₂ tension in alveolar air (mm. Hg.).

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THE FILLING OF SUBARACHNOID SPACES OVER THE CONVEXITY IN ENCEPHALOGRAMS OF NORMAL AND TUMOR CASES

By

ALEXANDER BONKALO, M.D.

The subarachnoid space of the convexity is represented in pneumograms by the air-filled sulci. The diagnostic value of insufflation of the subarachnoid spaces is generally underestimated because in the majority of cases pneumography is performed to determine whether or not an intracranial expanding process is present, and, therefore, attention is directed mainly to the ventricular system. Moreover, ventriculography rather than encephalography seems still to be used in many places when an expanding process is strongly suspected from the clinical examination.

Early investigators of encephalography were greatly interested in the examination of the convexity of the brain. (*Schott and Eitel, Schuster, Winkler, Jacobi and Winkler, etc.*). More recently *Davidoff* and *Dyke* have devoted a careful and very systematic study to the normal and pathological anatomy of subarachnoid spaces as demonstrated in roentgen pictures; a special technique in filling them has been suggested by *Belloni*; and, in his synopsis on encephalography, *Jantz* has presented some valuable information on subarachnoid spaces. The air-filled sulci were given more or less space in works dealing with roentgenology in psychiatric diseases (*Haugen and Hove, Wigert, Östergaard, Schiersmann, etc.*). *Larsby* and *Lindgren* have very clearly pointed out the sources of error in roentgenography of the convexity of the brain. *Lysholm* (1941) emphasized the great importance of subarachnoidal air in differential diagnosis between intra- and extracerebral tumors.

The extracerebral tumor wedges itself into the subarachnoid space, and as the top of the tumor depresses the brain surface, a more or less marked dilatation of the subarachnoidal cavity occurs, especially around the base of the tumor. Intracerebral tumors, on the other hand, increase the volume of the brain through infiltration or edema and may obstruct the subarachnoid space over the convexity

of an entire hemisphere. Although these facts are appreciated, the subarachnoid space over the convexity receives, with few exceptions, only passing mention in the literature on encephalography. The purpose of the present work has been to determine the conclusions which may be drawn from a closer examination of subarachnoid spaces shown on encephalograms taken without special regard to the filling of the convexity.

Material and Methods.

The material consisted of normal encephalograms and of encephalograms in cases of intracranial expanding processes. The former were a consecutive series selected at random from the roentgen archives of the Serafimer Hospital in Stockholm. By "normal" we mean that all cases showed a sufficient air-filling of the ventricular system and that there were no pathological changes according to our present knowledge of encephalography. The tumor series consisted of 102 cases of frontal and parietal expanding processes in which lumbar or suboccipital encephalography (not ventriculography) was carried out and in which sufficient air entered the ventricular system to secure a localization of the process. Only cases in which biopsy or autopsy confirmed the diagnosis were used. All pictures were taken with the uniform roentgen technique introduced by *Lysholm* and further improved by *Lindgren*, as a comparative estimation is possible only with the use of uniform technique. The air injection was not uniformly performed and will be further discussed later. The air-filled sulci over the frontal and parietal lobes were examined mainly on anteroposterior and lateral pictures taken with the patient in supine position. Attention was given to subarachnoid air only, and the filling of the subdural spaces was disregarded. "Air subarachnoidally situated is characterised by the sulci being well filled and by the fact that the air so located is difficult or impossible to dislodge by altering the posture of the head." (*Larsby* and *Lindgren*). Although oxygen was injected in almost half of the cases, it will be referred to as "air". The pictures of normal cases were classified according to subjective estimation of the air-filled sulci. In the classification of the material the quantity of the air and the length and width of the sulci were given equal consideration as the general conditions of the filling of the convexity were examined. Definitely pathological cases with enlarged ventricles or circumscribed atrophy over the convexity have been excluded from the normal material.

The data, such as age of patients, route and quantity of injected

air, have been tabulated separately and cross-referenced. As all data were not available in each case the totals sometimes vary in the several tables even though the same source material was used.

Comment and Discussion.

The subarachnoid space is a complicated, tortuous, non-rigid cavity which flexes with the changes in volume of the brain, such as pulsation, etc. The pathway and distribution of the air injected into this cavity is determined by several dynamic conditions. First of all air tries to rise in fluids. The position of the patient, the rate and sequence of draining liquor and injecting air (i.e. if the cisterns have collapsed or contain liquor), and the speed of injection are the primary technical factors which affect the distribution of the air in encephalography (*Robertson, Lindgren 1949*). That these factors may vary appreciably, in addition to variable endogenous factors, explains why repeated encephalography on the same patient may produce different subarachnoidal patterns (*Winkler, Jacobi and Winkler, Jantz, Tamura and Matsumura*). Notwithstanding these small variations in technique which may cause considerable variation in the resultant filling conditions, however, the comparison of the air-filled sulci in a series which has been examined with uniform roentgen technique but non-uniform insufflation methods may be of value in the drawing of some general conclusions.

I. Normal cases.

In Table 1 230 normal cases are classified according to degree of subarachnoid insufflation and according to air distribution between both sides. A complete absence of air-filled sulci with more

TABLE 1
Quantity and distribution of subarachnoid air over the convexity in normal cases.

Quantity of subarachnoid air over the convexity	Number of Cases	Distribution of subarachnoid air over both convexities	Number of Cases
No filling	4	Both sides equal	156
Little or uncertain	14	Right more than left	21
Average	109	Left more than right	21
Moderately increased	91	Uncertain	14
Increased	12		
Total	18 212	Total	212

or less air in the basal cistern was found in 4 cases only. In 14 cases the quantity of air over the convexity was very small. Among these were also those cases in which the bone structures (vascular channels, digital impressions, etc.) prevented exact estimation of filling conditions.

It is well-known that non-filling in encephalography despite suitable technique and especially non-filling of the ventricles occurs mainly under pathological conditions (*Ederle*, etc.). It may be added that the complete absence of surface filling with sufficient air in the basal cistern is so unusual that pathological conditions would be suspected. In addition it is shown in Table 1 that quantitative differences in the filling over both convexities are common in normal cases. There is no predilection for the right or left side. It should be emphasized that among the normal cases there were none with filling over one hemisphere and complete absence of filling over the other hemisphere.

In Table 2 the cases are classified according to degree of subarachnoid filling as opposed to: A. the age of the patient, B. the route of air-filling, and C. the quantity of air injected.

The age of the patient is of importance only in its relation to a certain degree to the width of the subarachnoid space. We may examine the more or less definitely physiological circumstances if we eliminate the two extreme groups in Table 2; that is, the one with little and the one with increased filling may be excluded. This has

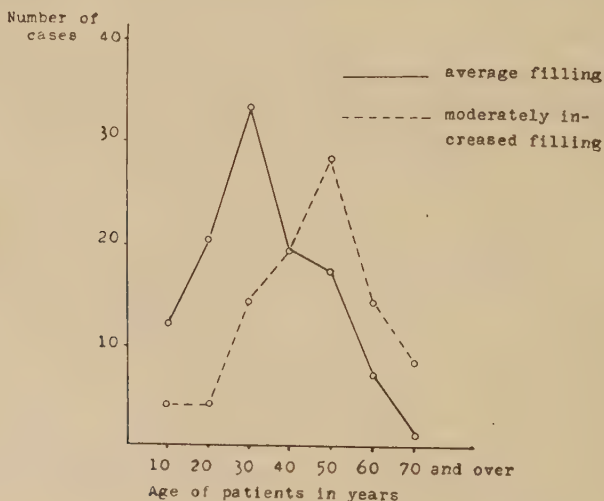


Fig. 1.

The distribution of normal cases with average and moderately increased filling according to age, showing the "physiological atrophy" of the brain as normal behaviour over the age of 40 years.

TABLE 2

Quantity of subarachnoid air-filling over the convexity, classified according to: A, the age of the patient; B, the route of injection; C, the quantity of injected air.

		No filling	Little or uncertain	Average	Moderately increased	Increased
A. Age of patient in years	0-10	1	2	12	4	—
	11-20	—	1	20	4	—
	21-30	1	2	33	14	2
	31-40	1	4	19	19	4
	41-50	1	4	17	28	—
	51-60	—	1	7	14	5
	60 >	—	—	1	8	1
	Total	4	14	109	91	12
B. Route of Injection	Subocc.	1	7	61	62	12
	Lumbar	2	5	41	23	—
	Total	3	12	102	85	12
C. Quantity of air injected in cc.	11-20	1	2	5	2	1
	21-30	2	7	33	31	4
	31-40	—	2	44	34	5
	41-60	—	—	7	11	1
	Total	3	11	89	78	11

been done in fig. 1, which graphically shows the distribution according to age of cases with average and moderately increased filling. (By average filling we mean those cases in which enough air-filling is found over the convexity to allow the forming of an opinion about the sulci, and in which these were not considered to be dilated.) The curve of cases with average subarachnoid space had a maximum at the age of 30 years; the one representing cases with moderately dilated subarachnoid space reaches a peak at 50 years. The point of intersection is at 40 years. This suggest that this age may mark the beginning of the more or less "physiological" atrophy of the brain. This age limit then might serve as a guide in the roentgen examination of psychiatric patients, establishing some principles helpful in the sometimes difficult diagnosis of doubtful cases of atrophy (Fig. 2). It should be noted that the generally accepted, and probably most reliable, symptom of atrophy in addition to dilatation of the ventricles is the widening of the sulci. On the other hand, the width of a sulcus as seen encephalographically depends upon its filling. A large

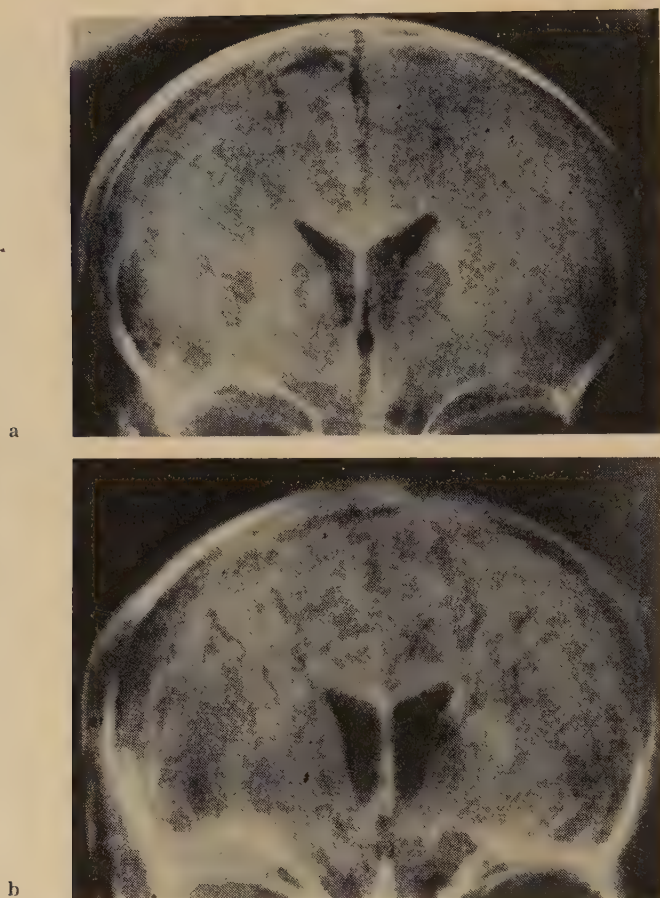


Fig. 2.

Examples of various filling conditions of the sulci over the convexity in normal cases. (a) "Average" filling, common pattern under the age of 40 years. (b) "Moderately increased" filling, common pattern over the age of 40 years.

quantity of air in a sulcus may give the appearance of dilatation while with a small quantity it may appear to be narrower (*Larsby and Lindgren*).

Part B of Table 2 shows the distribution of cases according to the quantity of subarachnoidal air over the convexity with reference to the lumbar or suboccipital route of injection. It must be emphasized, however, that the pathway of the air within the cranium depends first of all on the position of the head during injection and secondly upon the speed of the introduction of the air. Therefore part B of Table 2 is of limited value as no further details of the filling technique are known, but it does prove that a satisfactory filling over the con-

vexity may be obtained as well through suboccipital as through lumbar injection. However, in cases showing an increased quantity of subarachnoid air, suboccipital introduction prevails. An explanation of this might be that suboccipital encephalography is generally performed with greater speed than lumbar. Therefore, with the first method all of the air has not time enough to enter the ventricular system and a considerable amount may escape into the pontine cistern and through it farther on into the subarachnoid space.

Part C of Table 2 shows the distribution of cases with reference to quantity of air injected. It is evident that within the represented limits the quantity of air injected is not in marked proportion to the amount of air over the convexity. The distribution of air between the subarachnoid spaces and the ventricular system, therefore, depends not only upon the position of the patient and the speed of injection but also upon intracranial dynamic factors which vary individually. It very often appears that the air strives towards dilated subarachnoidal spaces. The result is that a circumscribed atrophy will be marked even in cases in which a relatively small quantity of air has been injected. The material investigated for this paper shows that a quantity of air between 20 cc and 40 cc fills not only the ventricular system but also the subarachnoid spaces sufficiently for diagnosis. Increasing the air quantity does not improve the result.

II. Expanding processes.

It is a well-known fact that dislocation of the cisterns and sulci may help in the localization of tumors even without filling of the ventricles.

TABLE 3

Distribution of subarachnoid air over the convexity in cases of expanding process.

	Extracerebral			Intracerebral		
	Frontal basal tumors	Meningiomas		Gliomas		Varia
		Para- sagittal	Con- vexity	Benign	Malignant	
Equal on both sides	4	4	1	3	—	—
Asymmetry over the convexity	2	5	4	11	2	2
No air over the tumor side	—	9	3	5	10	1
No air over the entire convexity	9	7	1	5	2	—
No subarachnoidal air at all	2	1	2	1	—	1
Uncertain	1	—	—	3	—	1
Total	18	26	11	28	14	5

The present examination deals only with the general filling conditions of the subarachnoid space on the convexity and with their diagnostic value. According to *Lysholm* (1941), the subarachnoid air is of great importance, being in many cases the only deciding factor in differential diagnosis between intra- and extracerebral tumors. *Lysholm* further writes: "Häufig kann man sogar verfolgen, wie diese über der Hirnoberfläche verbreitete Luft das Gewächs förmlich einhüllt, ja begrenzt, so dass man es unmittelbar wie mit blossen Auge zu sehen glaubt und sich eine Vorstellung von seiner Lage, Grösse und Form zu bilden vermag."

Among the 102 cases presented in Table 3, 55 were extracerebral tumors, 6 of which showed the peculiarity described in the preceding quotation from *Lysholm*, i.e. they were more or less outlined by air which partially enveloped the surface of the tumor. These cases follow:

Vgl. fr. 117. ♂ 57 years. Anamnesis: 1 year.

Op.: A global parasagittal meningioma the size of a goose egg was found under the bregma.

Rtg.: (30 cc air subocc.). Only the right ventricle was filled; it was dislocated to the left and depressed. The lateral side of the tumor was partly enveloped by air from the longitudinal fissure.

Vgl. fr. 33 ♂ 54 years. Anamnesis: many years.

Op.: Over the chiasma there was a tumor the size of a plum. Chromophobic adenoma.

Rtg.: (25 cc air subocc.). A bulging appeared in the lower part of the left anterior horn, which was displaced upwards and backwards. The tumor was partly covered by air over the medial side.

Vgl. fr. 74. ♂ 66 years. Anamnesis: 5 years.

Op.: Meningioma about the size of a hen's egg, arising from the anterior clinoid process of the left side.

Rtg.: (40 cc air subocc.). The left ventricle was somewhat dislocated to the left. The foremost and inferior parts of the anterior horns were put apart. A tumor was bulging in between the horns and was well characterized, enveloped by air, on a-p. pictures. (Fig. 3).

Vgl. fr. 91. ♀ 66 years. Anamnesis: 1 year.

Op.: Olfactory meningioma, the size of a goose egg.

Rtg.: (50 cc liquor removed suboccipitally, insufflation of 20 cc air + spontaneous air-filling). Upward displacement of the anterior horns. The superior and posterior surfaces of the tumor were covered by air. (Fig. 4).

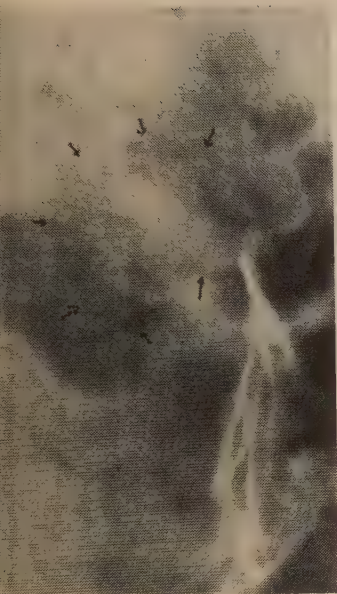
Vgl. fr. 233. ♂ 56 years. Anamnesis: 10 years.

Op.: Olfactory meningioma, the size of half a tangerine.

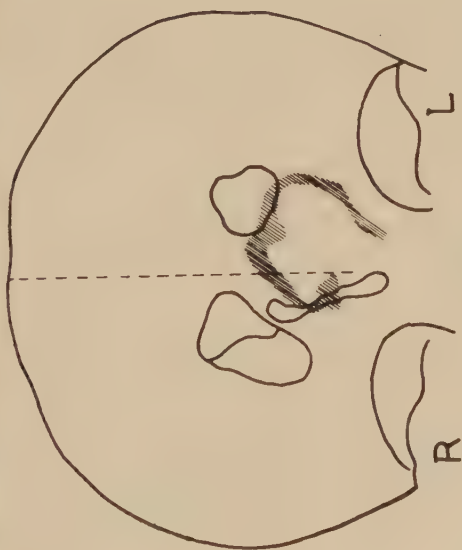
Rtg.: (40 cc air subocc.), Two irregular cavities in the frontal poles, which



a



c



b



d

Fig. 3.

A meningioma of the anterior clinoidal process enveloped by air is bulging in between the anterior horns. (a) Anteroposterior picture in supine position. (b) Sketch of (a). (c) Lateral picture in the same position as (a). (d) Sketch of (c); the ventricular system composed from several lateral pictures of the same case. The dotted line shows the left anterior horn. (Cf. case Vgl. fr. 74., in the text.).

appeared to communicate with the ventricle system. Both frontal horns were somewhat deformed and displaced upwards. The size of the tumor was made clearly visible by air enveloping the superior and posterior surfaces of the tumor.

Vgl. fr. 246. ♀ 39 years. Anamnesis: 3 years.

Op.: Suprasellar meningioma, the size of a hazelnut.

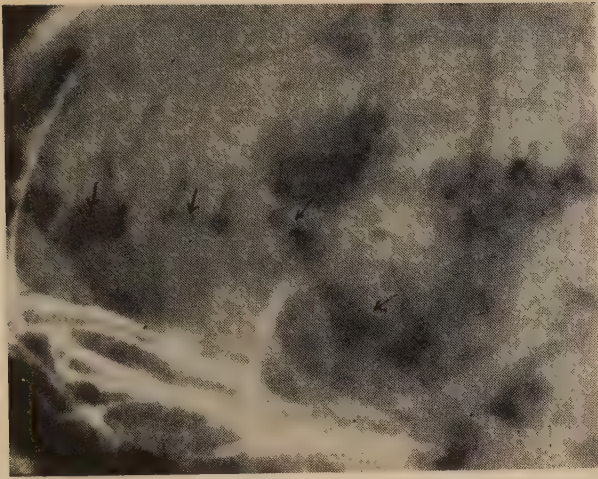
Rtg.: (30 cc air subocc.). The right anterior horn was somewhat displaced upwards and pressed inwards from below. Much air diffused around the tumor permitted an estimate of the size of the tumor on sagittal pictures.

Summarizing the foregoing cases: one was a parasagittal tumor, 5 were frontal basal. This means that from the 11 convexity meningiomas in Table 3 none was included; from 26 parasagittal meningiomas, 1 was included; from 18 subfrontal tumors (from intra- and suprasellar tumors those which showed a subfrontal extension were included in this material) 5 (28 per cent.) were partly enveloped by subarachnoidal air. It is commonly characteristic of these cases that the tumor is situated more or less in the midline and in the pathway of the air streaming from the basal cisterns to the convexity. It is thus, indeed, in the proximity of or partially inside the cisterns. In the case of the subfrontal tumor the air covers the tumor mainly from behind where it is trapped in its passage between the frontal lobes from the cisterna laminae terminalis towards the subarachnoid spaces of the frontal convexity and cisterna corporis callosi.

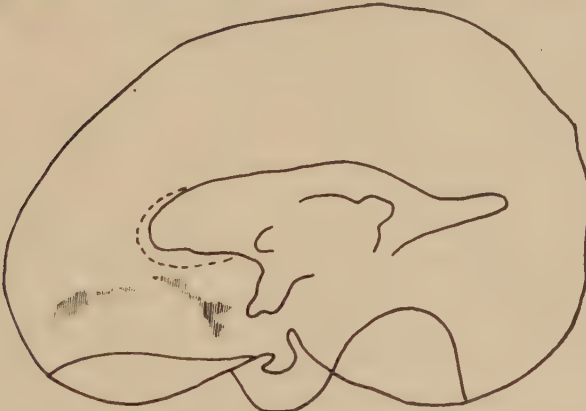
With the head not bent forward, but erect or even flexed somewhat dorsally, the air passes through cisterna pontis to cisterna chiasmatis and continues upwards. *If allowance is made for a certain quantity of air to pass this way during the injection, we have the best possibility of obtaining roentgenograms with good air-filling around a subfrontal tumor.*

In the case of the intracerebral expanding process, the volume of a lobe or an entire hemisphere increases, thereby decreasing the subarachnoid space. This is one reason for asymmetry in the air-filling over the convexities. A further reason may be the alteration in the consistency and elasticity of the tissue of a lobe or an entire hemisphere caused by tumor infiltration, edema, etc. As this alteration in consistency and elasticity changes dynamic factors which influence the air-filling (Robertson 1946, 1947), it may also be among the causes of asymmetric filling over the convexities.

In Table 3, 47 intracerebral tumors are represented. What conclusions may be drawn from this routine material as to the value of differences in filling over the convexity in differential diagnosis of intracranial tumors? A simple asymmetry, that is, less air on the



a



b

Fig. 4.

The inside surface of an olfactory meningeioma entirely outlined by subarachnoidal air. (a) Lateral picture in supine position. (b) Sketch of (a); the ventricular system composed from several lateral pictures of the same case. The dotted line shows the right anterior horn. (Cf. case Vgl. fr. 91., in the text.).

side with the tumor, is such a common finding, of course, that it has no diagnostic value. If in addition to the tumor there is an atrophy, filling may be increased on the convexity over the involved hemisphere. In this series there was only one case, an arterio-venous aneurysm, with a marked filling difference of the latter type. *Lys-holm* has (1941) emphasized that atrophy on the same side as an expanding process indicates an arterio-venous aneurysm.

Although the presence of less air on the tumor side might indicate any type of tumor, there is one peculiarity shown in Table 3 which is worthy of consideration: the behaviour of malignant gliomas.

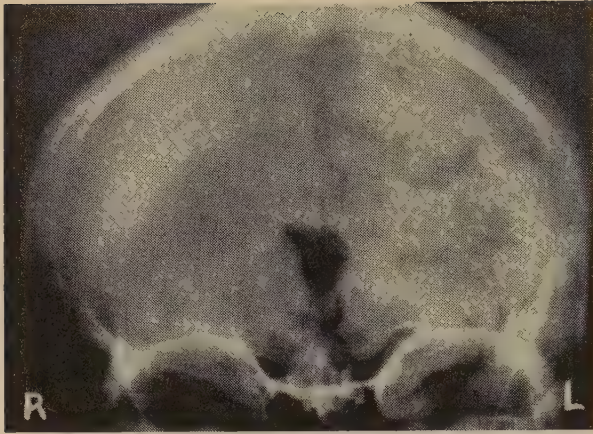


Fig. 5.

Glioblastoma in the right motor region. A complete lack of subarachnoid filling over the hemisphere on the tumor side in addition to a marked filling over the normal side. (♀ 54 years. Anamnesis: 3 months. Encephalography with 30 cc air suboccipitally.).

Among 14 cases there were 2 cases with no convexity air, 2 more with filling over both hemispheres but with marked difference between both sides. In 10 cases (70 per cent.), there was no convexity air over the tumor side with more or less filling on the normal side (Fig. 5). Histologically all of these cases were shown to be glioblastomas, tumors which in addition to being strongly infiltrative growths are most inclined to produce edema. This means that with glioblastomas there is an alteration of the brain tissue which extends to almost an entire lobe or hemisphere. *This* alteration appears on roentgenograms as asymmetry in the air-filling over the convexity. It may be concluded, accordingly, that if encephalographic findings on the ventricular system indicate a tumor and the air-filling of the sulci is asymmetric, the case may be any kind of expanding process, but that, with symmetric filling over both hemispheres, it is very probable that the tumor is *not* a glioblastoma. In other words, this means that the degree of difference in filling over both sides may be taken into consideration as an indication of malignancy in qualitative diagnosis of intracerebral tumors.

Survey of Results and Conclusion

The subarachnoid space over the convexity was examined on encephalograms showing satisfactory filling of the ventricles in 230 normal cases and 102 cases with intracranial expanding processes.

I. Normal cases.

(1) In 4 cases out of 230 (1.7 per cent.) there was no air over the convexity in addition to filling in the basal cistern. In 14 cases (6.1 per cent.) subarachnoid filling was slight or uncertain. Of the remaining 212 cases with good subarachnoid air-filling over the convexity, 156 cases (73.6 per cent.) showed equal distribution of air over both hemispheres. A marked predilection for one side was present in 42 cases, 21 (9.9 per cent.) for the right and 21 (9.9 per cent.) for the left. In 14 cases (6.6 per cent.) the existence of a difference was uncertain.

(2) A widening of the subarachnoid space over the convexity was the common finding in encephalograms of patients over 40 years of age.

(3) A filling over the convexity which allows an estimation of the width of the sulci may be obtained as well through the suboccipital as through the lumbar route and is more or less independent of the quantity of air injected. However, most of the cases showing increased subarachnoidal filling over the convexity were suboccipitally insufflated.

II. Expanding processes.

(1) Direct outlining of an extracerebral tumor by the subarachnoid air was found only in cases of midline tumors situated in the proximity of the cisterns. With the exception of one, all the cases found were subfrontal tumors, for the most part olfactory meningiomas. This peculiarity of subfrontal tumors may have diagnostic value in roentgenological examination with the use of a suitable technique.

(2) Marked increase of subarachnoid filling over the tumor side was found in only case, which was an arteriovenous aneurysm.

(3) Subarachnoid filling over the convexity varies considerably in cases of intracerebral tumor. An asymmetry in the filling over both hemispheres is proportionate to a certain degree to the histological malignancy of the tumor. Glioblastoma may be excluded from consideration in differential diagnosis if the subarachnoid space over the convexities is equally filled.

In conclusion it must be emphasized that observation, even of routine material, proves that close attention to the subarachnoid space may appreciably increase the diagnostic value of encephalography and that with a suitable technique, adapted to certain cases, it may be still further increased.

I want to express my great indebtedness to Professor E. Lindgren for his valuable suggestions and for the use of the material of the Roentgen Department, Serafimer Hospital.

SUMMARY

An examination was made of the subarachnoid spaces over the convexity on a routine series of encephalograms taken in normal and tumor cases. Asymmetry was found to be common in normal cases, and a more or less physiological dilatation of this space was observed to begin with the age of 40 years. Some factors of the filling were discussed. It was found that extracerebral tumors, especially subfrontal tumors, may be outlined by air. It was emphasized that a difference in filling of the sulci over both hemispheres might be taken into consideration in differential diagnosis of intracerebral tumors.

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PERSONALITY ATTITUDE AND PHYSICAL MAKE-UP

By

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Kretschmer's book "Körperbau und Charakter" (1) gave rise to much discussion and stimulated research which in course of time resulted in the elaboration of suitable clinical methods permitting the objective evaluation of the physical make-up. In 1937 the Dane *Strömberg* (2) described a simple method for determining the physique of an individual and expressing it in the form of an index. This index has been used in the present study, in which it was desired not only to define the individual physical make-up more precisely, but also to obtain a clearer conception of the various types of personality. *Kretschmer's* division of personalities into schizoid and cycloid types was too crude for the purposes of the present study. The criss-cross combinations of attitudes seen in some individuals will not permit the assignment of the latter to either of these two groups. It was therefore decided to use *Sjöbring's* personality analysis (3, 4, 5), which permits the classification of personalities made up of a varying combination of several well-known fundamental characteristics.

Strömberg's index for designating the type of physical make-up is deduced from the height of the patient, the breadth of the chest, and the depth of the chest. In order that the indexes of the males might be comparable to those of the females we used two different correction factors, one for each sex.

The great advantage of typing personality ad modum *Sjöbring* is that the components of a given personality may be analyzed along four "lines" which together cover the attitudes of normal combinations. The variations along any one of these four lines is said to occur independently of variations in any of the other lines.

In the present study one of the lines included different degrees of syntonía as conceived by *Bleuler*. The syntonía type of personality is almost identical with what *Sjöbring* describes as "sub-stable". The

"syntonia line" in this study will therefore provide for three degrees of personality attitude, namely "non-syntonic", "slightly syntonic", and "markedly syntonic". The slightly syntonic attitude is characterized by distinct syntonic traits which, however, are not so pronounced as in the markedly syntonic. Instead of the lines "validity" and "solidity" used by *Sjöbring* we have employed different degrees of "psychasthenia" and "hysteria" as conceived by *Janet*. These personality components have likewise been graduated into three degrees, namely non-, slightly, and markedly asthenic and hysteric, respectively. The "intelligence line" adopted here coincides with *Sjöbring's* "capacity line" and has been graduated into high, normal, and inferior grades.

The physical make-up of the group of individuals conceived as schizoid were analysed partly on the basis of these four lines and partly independently of the pattern.

The Syntonic Attitude.

Such personality traits as natural sociability—ease to make friends and retain them, compassionateness, sensitivity to criticism and praise, failure, and success, nature-workship, cleverness in practical affairs, and spontaneous changes in mood have been regarded as cardinal components of the syntonic attitude.

The Psychasthenic Attitude.

Fastidiousness, pettiness, fickle-mindedness, bashfulness, fundamental insecurity, nervous tension when faced with new situations or in the presence of superiors, habit slavery, readiness to feel harassed and pushed, and inordinate fatigue have been regarded as typical components of the asthenic attitude.

The Hysteroid Attitude.

Such characteristics as impulsiveness, need for a change and merry-making and emotional sprees, pompousness and eloquence, poor emotional control, strong imagination and suggestiveness and talent for acting, have been assigned to the hysteric type.

The Schizoid Attitude.

Suspiciousness, stubbornness, consistency, red-tapism, hard-heartedness, speculativeness, aloofness and a tendency towards isolation have been regarded as characteristics of the schizoid personality.

The present report is based on study of 1,000 in-patients treated in 1948 at the Psychiatric Clinic of Sahlgren's Hospital.

Most of the patients attending this clinic belong to the type of "neurotics", slightly mentally insufficient persons, encountered in the population of a large town. A few of them are women applying for interruption of pregnancy. Some of the patients are applicants for a medical certificate of their general condition of health to substantiate claims on insurance companies, mostly on account of some long-standing injury.

To permit a comparison of these patients they were examined by one and the same method devised by *Lindberg* (6, 7). This method or pattern is suitable both for clinical and scientific purposes. Every patient whose remarks could be relied upon was analyzed by this method unless his condition counterindicated such an examination. With the aid of the records from the department and from the out-patient department as well as of the curator's report the chief psychiatrist and his assistant tried to determine the patient's attitudes. As all the patients were analyzed in intimate cooperation with the chief psychiatrist and according to one and the same method a standardized evaluation of the attitudes may be presumed.

The physical make-up was determined by *Strömgren's* index independently of the type of attitude. In order to make the comparisons between different patients as reliable as possible all the measurements were taken and all the calculations of the indexes done by one and the same person, namely the laboratory assistant, who was specially trained for this purpose.

RESULTS

Strömgren's index comprises plus and minus values with the intermediate zero. Zero was originally intended to indicate the index value of persons who were neither pyknic nor leptosome. After the examination of a large population *Strömgren* (8) observed that this intermediate value ought rather to be about -0.4 unit. The discussion of this question, however, lies beyond the scope of the present study.

Another mean is the average index of all the people examined in a given population. In the present series this mean was -0.48 unit with a standard error of ± 0.017 unit. The present study, however, will show the insignificant value of such a general mean. If a mean is to be of any use, it must be calculated on the basis of the respective average value of the different personality attitudes. In the following the present series has been divided in this manner.

Asthenic Personality Attitude and Physical Make-up.

The above-mentioned index value of -0.48 units is the mean value of the whole material. If the present series is divided into different groups as regards degree of asthenia, the group "asthenic attitude" will have a mean value of -0.52 ± 0.023 whilst the corresponding value of the group "non-asthenic attitude" will be -0.36 ± 0.027 . The difference between the mean values of these two groups will be 4.6 times the standard error. Table I shows that on further division the group "slightly asthenic attitude" will have an index of -0.48 ± 0.034 on the average whilst the "markedly asthenic" group will have an index of -0.59 ± 0.030 . The difference between the mean values of the non-asthenic and the markedly asthenic and between the non-asthenic and the slightly asthenic is 5.8, respectively 2.8, times their respective standard errors, so that these differences are statistically significant. In view of the tendency exhibited by the series when divided in this manner the difference between the means of the markedly asthenic and the slightly asthenic must be regarded as statistically probable, in spite of the difference being only 2.4 times its standard error.

TABLE I
Degree of Asthenia and Strömgren's Index.

Degree of asthenia	Strömgren's index. Mean and standard error of the mean $M \pm \varepsilon M$	Difference between the means and standard error of the difference $D_M \pm \varepsilon D_M$	$D_M / \varepsilon D_M$
Non-asthenic attitude	-0.36 ± 0.027		
		$+ 0.12 \pm 0.043$	2.8
Slightly asthenic attitude	-0.48 ± 0.034		
		$+ 0.11 \pm 0.045$	2.4
Markedly asthenic attitude	-0.59 ± 0.030		

Broadly speaking, one may at this stage of the study say that an asthenic attitude is bound to a physical make-up of lower index value than is a non-asthenic attitude. The index of the physical make-up seems to decrease with increasing degree of asthenia.

Intelligence and Physical Make-up.

Table II shows a comparison of intelligence and physical make-up.

TABLE II
Degree of Intelligence and Strömgen's Index.

Degree of intelligence	Strömgen's index. Mean and standard error of the mean $M \pm \varepsilon M$	Difference between the means and standard er- ror of the difference $D_M \pm \varepsilon D_M$	$D_M / \varepsilon D_M$
High intelligence	-0.42 ± 0.055	$+ 0.09 \pm 0.058$	1.6
Normal intelligence	-0.51 ± 0.022	-0.09 ± 0.064	1.4
Inferior intelligence	-0.42 ± 0.060		

It will be apparent from Table II that there is no correlation between the standard of intelligence and physical make-up determined by means of *Strömgen's* index.

Hysteric Attitude and Physical Make-up.

When the series was divided according to the degree of hysteria, those persons belonging to the hysteric group were found to have an index of -0.50 ± 0.025 . The corresponding figure of the non-hysteric group was -0.46 ± 0.031 . There was thus no significant difference between these two groups. Table III shows that a further division of the hysteric group does not alter the result either.

TABLE III
Degree of Hysteria and Strömgen's Index.

Degree of hysteria	Strömgen's index. Mean and standard error of the mean $M \pm \varepsilon M$	Difference between the means and standard er- ror of the difference $D_M \pm \varepsilon D_M$	$D_M / \varepsilon D_M$
Non-hysteric attitude	-0.46 ± 0.031	-0.02 ± 0.047	0.4
Slightly hysteric attitude	-0.44 ± 0.035	$+ 0.13 \pm 0.049$	2.7
Markedly hysteric attitude	-0.57 ± 0.034		

There is thus no apparent difference between the hysteric and non-hysteric types as far as the index for physical make-up is concerned.

Syntonic Personality Attitude and Physical Make-up.

In the study of the physical make-up of individuals of the syntonic type it was found advantageous to make a distinction from the very beginning between the markedly syntonic and the slightly syntonic types. The reason for this early distinction will be obvious later in this paper. In Table IV the series has accordingly been divided into three groups. The non-syntonic have a physical make-up index of

TABLE IV
Degree of Syntonia and Strömgen's Index.

Degree of syntonia	Strömgen's index. Mean and standard error of the mean $M \pm \varepsilon M$	Difference between the means and standard error of the difference $D_M \pm \varepsilon D_M$	$D_M / \varepsilon D_M$
Non-syntonic attitude	-0.64 ± 0.049		
Slightly syntonic attitude	-0.58 ± 0.031	$+0.06 \pm 0.058$	1.0
Markedly syntonic attitude	-0.38 ± 0.027	-0.20 ± 0.041	4.9

-0.64 ± 0.049 , the corresponding value for the slightly syntonic and markedly syntonic being -0.58 ± 0.031 and -0.38 ± 0.027 , respectively. There is thus a significant difference between the non-syntonic and markedly syntonic as well as between the slightly syntonic and the markedly syntonic. There is, however, no significant difference between the non-syntonic and the slightly syntonic, the difference here being only once the standard error.

The markedly syntonic personalities thus seem to differ physically from the non-syntonic and the slightly syntonic, the first group having a higher mean value of *Strömgen's* physical make-up index than either of the two. The mean value of the physique of the non-syntonic and the slightly syntonic, respectively, did not differ significantly in the present series.

Schizoid Traits and Physical Make-up.

Those persons who displayed pronounced schizoid traits—in the sense of the term described on page 340—had a physical make-up

index of -0.60 ± 0.056 whilst those without such traits had an index of -0.48 ± 0.020 . The difference between these two groups is 2.1 times the standard error and is thus statistically significant. This difference is, however, in need of an explanation, which will be given later in this paper.

Combination of Different Attitudes and Physical Make-up.

The studies described in the previous section permitted us to form a rough idea of the relationship between the different personality attitudes and physical make-up. The investigation was, however, incomplete in so far as it made no allowance for the fact that the

TABLE V
Degree of Asthenia and Syntonia and Strömberg's Index.
(Mean and standard error of the mean).

	Non-syntonic attitude	Slightly syntonic attitude	Markedly syntonic attitude
Non-asthenic attitude	-0.59 ± 0.101	-0.52 ± 0.058	-0.21 ± 0.054
Slightly asthenic attitude	-0.68 ± 0.094	-0.67 ± 0.048	-0.36 ± 0.048
Markedly asthenic attitude	-0.63 ± 0.100	-0.64 ± 0.052	-0.54 ± 0.033

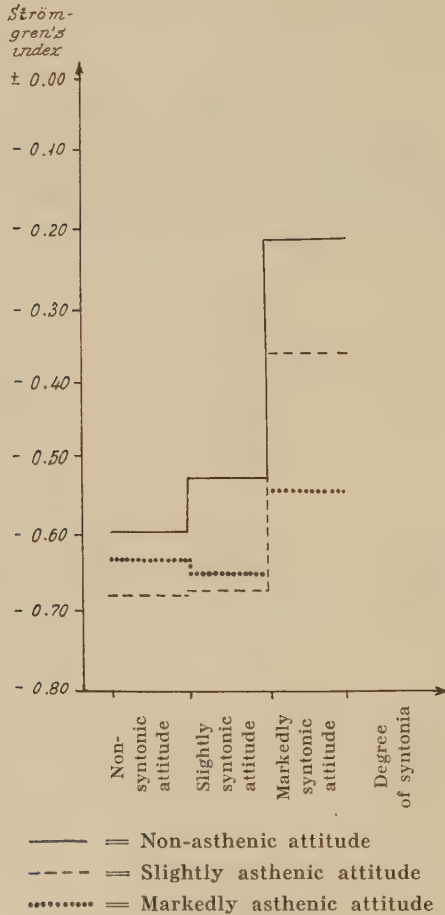
combination of different personality attitudes is capable of variations in index value. When a person of somewhat asthenic type may also be regarded as somewhat syntonic, we must also examine whether and in what respect a given combination will affect the physical make-up. From the earlier sections in this paper it will be apparent that the degree of intelligence and the degree of hysteria do not seem to be tied up with or bound to variations in the physical make-up as measured by *Strömberg's* index. Therefore in what follows we may concentrate our interest solely on the effect of asthenic and syntonic combinations on the physique. The different combinations and corresponding *Strömberg's* index have been tabulated in Table V.

Table V shows that, as pointed out above, a marked syntonic attitude has a higher index value than the non-syntonic or slightly syntonic. This is readily seen in Fig. 1.

Marked syntonia increases the index of all the degrees of asthenia.

This increase is greatest in non-asthenic and in the slightly asthenic groups. It will, moreover, be apparent from Fig. 1 and Table V that an increased degree of asthenia lowers the value of the index. This

Figure 1.
Degree of Asthenia and Syntonia and Ström-gren's Index.

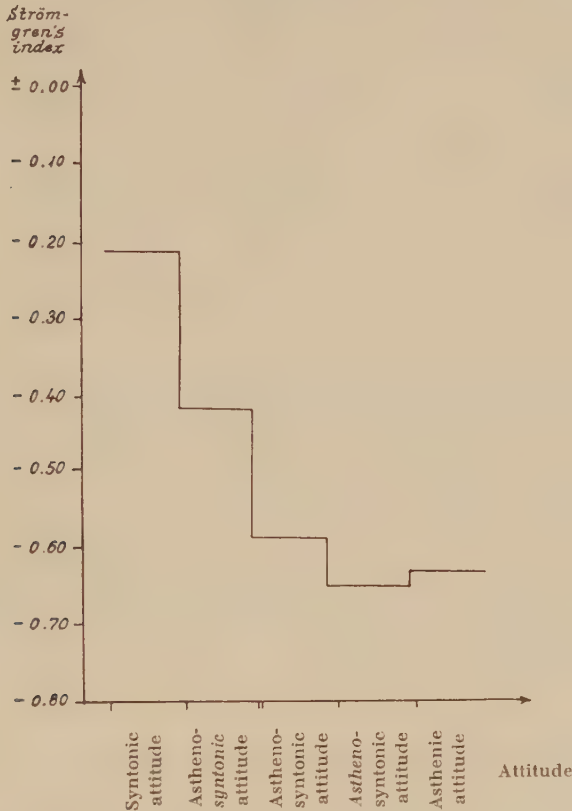


applies above all to those personalities that are at the same time markedly syntonic. The difference in index between the non-asthenic and the markedly asthenic who are at the same time markedly syntonic is + 0.33 index unit. This difference is 5.2 times the standard error and is therefore significant. The difference diminishes considerably with decreasing degree of syntonia, but is nevertheless present. Fig. 1 shows that in personalities which are both markedly syntonic

and markedly asthenic the index of the physical make-up is lower than it would have been in the absence of asthenia. This means, then, that increasing degree of asthenia is accompanied by a decreasing

Figure 2.

Ström-gren's Index in Different Degrees of Syntonic-Asthenosyntonic-Asthenic Personality Traits.



index. Fig. 2 shows how a predominance of asthenic and syntonic traits, respectively, will affect the index.

Sex, Personality Attitude, and Physical Make-up.

In the preceding section the index values were determined independently of sex. That sex may be disregarded will be apparent from Table VI, where the indexes of the personality attitudes have been determined separately for each sex.

TABLE VI
Sex Differences and Strömgren's Index. Syntonic and Asthenic Attitude.

	Sex	Non-syntonic attitude	Slightly syntonic attitude	Markedly syntonic attitude
Non-asthenic attitude	♂	-0.52 ± 0.192	-0.48 ± 0.074	-0.23 ± 0.068
	♀	-0.56 ± 0.126	-0.64 ± 0.086	-0.18 ± 0.048
	Diff.	$+0.04 \pm 0.230$	$+0.16 \pm 0.113$	-0.05 ± 0.108
Slightly asthenic attitude	♂	-0.70 ± 0.093	-0.56 ± 0.069	-0.33 ± 0.058
	♀	-0.81 ± 0.121	-0.68 ± 0.057	-0.44 ± 0.067
	Diff.	$+0.11 \pm 0.153$	$+0.12 \pm 0.089$	$+0.11 \pm 0.089$
Markedly asthenic attitude	♂	-0.69 ± 0.109	-0.60 ± 0.078	-0.51 ± 0.076
	♀	-0.56 ± 0.164	-0.66 ± 0.069	-0.54 ± 0.041
	Diff.	-0.13 ± 0.197	$+0.06 \pm 0.104$	$+0.03 \pm 0.086$

The table shows that the difference between the sexes is nowhere greater than 1.4 times the standard error. Sex is thus unimportant here. This is also as was expected because, as mentioned above, the index had already been corrected for sex. The result of the investigation also confirms that the correction was fully adequate and that the index values of the men and women are comparable. Also the personality attitudes were determined independently of sex. Table VI therefore also confirms that the examination technique permits a rather exact assignment of personalities of either sex into groups which permit of reliable comparison.

Age, Personality Attitude, and Physical Make-up.

It is generally accepted that the physical make-up of most people changes between 40 and 50 years of age and that the individual then begins to put on weight. This change makes it necessary to study the effect of age on the index. Owing to the composition of the present series the examination could not be made on the basis of the material as a whole because the syntonic personalities were somewhat predominant in the higher age groups (71 per cent over 45 years of age were syntonic, but only 46 per cent under this age). This means then that here, too, the various combination types must be analysed separately. In this analysis, as before, the personalities were dealt with according to the degree of asthenia and syntonia, respectively. The results are shown in Table VII.

TABLE VII

Age and Strömgen's Index, Syntonic and Asthenic Attitude.

	Under 41 years old $M < 41 \pm \epsilon M$	$M_{41-50} \pm \epsilon M_{41-50}$	Above 50 years old $M > 50 \pm \epsilon M$	$D_M < 41 - M > 50$		$D_M < 41 - M_{41-50}$	
				ϵD	ϵD	ϵD	ϵD
Non-asthenic, non- or slightly syntonic attitude	— 0.58 ± 0.067	— 0.51 ± 0.104	— 0.31 ± 0.109	2.1	0.6	1.3	
Non-asthenic, markedly syntonic attitude	— 0.35 ± 0.084	— 0.21 ± 0.117	— 0.13 ± 0.089	1.8	1.0	0.5	
Slightly asthenic, non- or slightly syntonic attitude	— 0.70 ± 0.055	— 0.39 ± 0.089	— 0.28 ± 0.117	3.2	3.0	0.7	
Slightly asthenic, markedly syntonic attitude	— 0.51 ± 0.052	— 0.04 ± 0.122	— 0.14 ± 0.091	3.5	3.6	0.7	
Markedly asthenic, non- or slightly syntonic attitude	— 0.70 ± 0.050	— 0.54 ± 0.111	— 0.38 ± 0.131	2.3	1.3	0.9	
Markedly asthenic, markedly syntonic attitude	— 0.63 ± 0.037	— 0.33 ± 0.133	— 0.24 ± 0.123	3.0	2.5	0.5	

TABLE VIII
Age, Sex, and Strömgen's Index.

	Strömgen's Index					
	< 41 years		41-50 years		> 50 years	
	♂	♀	♂	♀	♂	♀
Non-asthenic, non- or slightly syntonic attitude	— 0.50	— 0.56	— 0.60	— 0.60	— 0.19	— 0.53
Non-asthenic, markedly syntonic attitude	— 0.37	— 0.25	— 0.17	— 0.35	+ 0.09	— 0.06
Slightly asthenic non- or slightly syntonic attitude.....	— 0.81	— 0.80	— 0.41	— 0.38	— 0.20	— 0.41
Slightly asthenic, markedly syntonic attitude	— 0.71	— 0.63	+ 0.02	— 0.09	— 0.11	— 0.18
Markedly asthenic, non- or slightly syntonic attitude.....	— 0.66	— 0.66	— 0.65	— 0.35	— 0.43	— 0.34
Markedly asthenic, markedly syntonic attitude	— 0.55	— 0.63	— 0.49	— 0.36	— 0.33	— 0.27

The earlier observation that an increased degree of asthenia lowers the index and that an increased degree of syntonía increases the index was confirmed also in this table. This relationship between the degree of asthenia and index and degree of syntonía and index thus holds good for all age-groups. It is readily seen from the table that there is a difference between the index of persons under 41 years of age and those over 50. This difference attains statistically significant values only in 50 per cent of the cases, but the order of the difference in the other cases is such as to warrant the assumption that an examination of the problem in a larger series would show this difference to be statistically significant. It also seems as if the index value changes nearer 40 than 50 years of age. Another tendency which might possibly be inferred from the present investigation is that the difference in index due to age and apparent in all personality attitudes is somewhat more marked in asthenics.

In the preceding section it was shown that the index values of the various personality groups were the same in both sexes. But when viewing Table VII one might ask whether the difference in index due to age is in any way directly connected with the climacteric of the women. Unfortunately the material is too small to permit anything

but very cautious and tentative interpretations. In Table VIII the series is divided according to sex. The present series is, however, too limited to permit statistical calculations, for which reason the means have been given without the standard errors.

It will be apparent from Table VIII that it is not a change in the women's indexes alone that is responsible for the demonstrated difference due to age. This difference is just as often dependent upon changes in the men's indexes. It is therefore justifiable to conclude that index changes due to age are not attributable solely to the climacteric.

DISCUSSION

The division of personality attitudes adopted by *Kretschmer* was found too schematic to cover all the criss-cross combinations encountered in the human psyche. The more detailed differentiation made possible by the methods we adopted in the present study proved to answer the purpose much better.

Results of examinations of a series of the present type have their limitations. Like *Kretschmer's* studies, they were based on a series that cannot be regarded as consisting of normals. It should be borne in mind that when the patients appeared for examination we always tried to ferret out the personality attitudes they possessed before they became neurotic, i.e. their fundamental "normal" attitudes. Moreover, the patients examined had been cared for at the hospital for such mild insufficiency conditions as would probably generally be regarded as mild neuroses.

The above objection that might be raised against the nature of the series and the results of the investigation would perhaps be more justified if we had attempted to identify a certain personality attitude with a certain type of physical make-up. But the objection can be practically ruled out if we try to discern or define a type of physical make-up peculiar to a given personality attitude. It is in this last respect and only in this respect that the author feels justified in drawing general conclusions.

Strömberg's index for determining and classifying the types of physical make-up was originally intended for mathematically dividing people into leptosomes and pyknics. In this index minus values suggest a leptosome physique, plus values a pyknic physique. In other words the lower the index, the more leptosome is the personality, and the higher the index, the more pyknic. It was also in the light of this fact that a comparison of the indexes of different personality attitudes was believed to be valuable.

In conformity with *Kretschmer's* studies the physical make-up of the syntonic personality was more pyknic than that of the non-syntonic, i.e. the syntonic had a higher index value. This physical difference measured by index units was striking. It was present and equal in both sexes. The difference in physical make-up between the syntonic and non-syntonic types was present irrespective of age, and the difference between corresponding ages was constant. On the other hand, the index value of one and the same attitude was found to vary with age. This variation, which is practically independent of the personality attitude, incurred a higher index for persons over 50 years of age than for individuals under 40. This point will be discussed below. A remarkable observation was that the attitude bound to the higher indexes was the markedly syntonic, whilst the index of the slightly syntonic attitude did not differ significantly from that of the non-syntonic type. This might possibly be explained by the heterogeneity of the slightly syntonic group, which therefore included more non-syntonic individuals than it ought to. This explanation, however, seems improbable. Another explanation might be that many individuals are capable of having distinctly syntonic traits without their physique necessarily being pyknic. A third explanation might be that the group of slightly syntonic may include more asthenic personalities than the markedly asthenic group, which group is bound to a lower index. This explanation must, however, be refuted, because the investigation showed that the difference between the slightly syntonic and markedly syntonic was uniform independently of the degree of asthenia.

As mentioned above, the asthenic attitudes have a lower index than have the non-asthenic. It also seems as if the degree of asthenia is conversely proportional to the index value. The decrease in index of the markedly asthenic seems to be smaller than the increase in index seen in marked syntonia. As was the case with the syntonic, sex had no influence on the variation of the index of the asthenic. The variation of the index value according to the varying degree of asthenia also seemed to be independent of age. There was, however, an absolute variation of index, i.e. the index value increased as age advanced. This variation was on the whole independent of the earlier personality attitude.

Between the ages of 40 and 50 years the physique becomes more pyknic and thereby involves a variation of the index at this age. The difference in index may of course also be explained by a change in the physical changes of the older generation. But this assumption seems improbable, because the variation is limited to a period shorter than

a decennium. It would therefore seem as if the explanation should be sought rather in the physical changes an individual is likely to undergo between the age of 40 and 50 years. It seems hardly probable that this variation in index should be directly related to the climacteric in women because the index variation occurs irrespective of sex. One is tempted to attribute the variation to the formation of fat in the subcutaneous tissue in these ages. This means, then, that the cause of the variation in index is due to changes in the manner of living and metabolic processes in middle age. This view is also supported by the fact that the index of the markedly asthenic varied more than that of the non-asthenic, the former being those whose habits and manner of living on the whole change most in middle age. One factor contributing to the leanness of the psychasthenic is the well-known restlessness of this type. It is likewise known that a number of asthenic symptoms decrease with advancing years, particularly, for example, nervous restlessness, which is often pronounced in youth. This alone, then, may contribute towards or even be responsible for the gradual accumulation of fat in asthenics approaching middle age.

Kretschmer thought the leptosomatic physique to be linked to schizoid traits or attitudes. He used the term schizoid in a much wider sense than we have done here. Even though it is not possible to endorse *Goldkuhl's* (9) view that *Janet's* conception of psychasthenia coincides with *Kretschmer's* idea of a schizoid personality, it cannot be denied that the scope of the word as used by *Kretschmer* covers several obviously psychasthenic variants. In the present series the index of the persons with schizoid traits—according to *Kretschmer's* concept—came closer to the leptosomatic type than did the indexes of non-schizoids. The difference was, however, only twice the standard error, so that it was not significant. It is also obvious that this difference is not real, because the schizoid group consisted of more individuals with an asthenic attitude than did the non-schizoid group, the percentage being 76.2 and 70.4, respectively. Still more striking, however, is the fact that the schizoid group consisted to 30 per cent of markedly syntonic individuals, whilst the corresponding percentage in the non-schizoid group was 52.3. The above-mentioned factors are of such an order that they alone are surely sufficient to explain the difference in index between individuals with schizoid and those without schizoid traits. From this it may be inferred, then, that schizoid personality attitudes are not necessarily linked to a leptosomatic physique. Unfortunately the series is too limited (80 individuals with schizoid traits) to make a more complete analysis.

SUMMARY

One thousand patients treated at the Psychiatric Clinic of Sahlgren's Hospital, Gothenburg, were examined as regards physical make-up as expressed by *Strömgren's* index and as regards syntonie, asthenic, and hysteric personality attitudes and combinations thereof ad modum *Sjöbring*. The study revealed that the physical make-up of markedly sytonic individuals is more pyknic than is that of non-sytonic types. On the other hand, a psychastenic personality attitude causes the index to shift in a leptosomatic direction. These shifts were independent of sex. The index, however, changed with advancing age, so that *Strömgren's* index increased in middle age irrespective of personality attitude. This index shift occurred between the ages of 41-50 years.

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MENINGO-ENCEPHALO-MYELITIS
IN A PATIENT WITH HYPERGLOBULINEMIA AND
ALLERGIC SYMPTOMS FROM THE SKIN
AND JOINTS¹

By

OLE ESMARCH, M.D.

In the literature I have been unable to find descriptions of similar syndromes. According to the history and clinical examination it would seem most natural to suppose that it is a case of a delimited pathological unit with reaction from various organs, and not a case of various parallel affections.

For the sake of clarity I prefer to give the long history in detail and at the same time give some hints as to the diagnostic problems, while confining myself to a brief discussion of the case.

The patient is an unmarried female photographer's pupil aged 20.

Nothing could be learnt about familial predispositions, though it must be mentioned that a brother of the patient suffers from an Ostitis fibrosa localisata. One sister had "lain on a board" at home, but no information could be gained of the non-traumatic disease of the spine, which has been quite cured. Another sister is in good health.

The patient's father is a man who is interested in different forms of agricultural activities. She is no. 4 of 4 children. After leaving school she was for a year apprenticed to a photographer. In addition she helped her father with farm work, mill work, and horse-breeding, especially training.

The present affection has manifested itself periodically since the age of five. Between the attacks she has felt quite well. As far as can be judged, her bad periods have covered half the time. Nevertheless at an age of 15 she passed the middle school exam with credit, not having been more than the usual time in each class.

From her 15th year she has had her menstruation somewhat irregularly, the intervals being from 3 to 5 weeks, the duration 3 days.

Is stated never to have had infectious diseases, such as severe cases of influenza,

¹ Lecture delivered at the Danish Neurological Society, on Jan. 26, 1949.

angina, otitis media, infections of the urinary passages, rheumatic fevers, affections of the liver, affections of the glands, pneumonia, or pleuritis.

Never asthmatic attacks or hay fever. Easily gets red eyes, especially during threshing. Working with horses does not affect her.

Since the age of 5 there have been periods of sickness with a rapidly arising painful swelling of one or more joints, often passing from one joint to another. The attacks are without fever, not accompanied by fatigue, and last from some hours to as much as 1.5 months. The intervals vary from a couple of days up to one year. All joints, small as well as large ones, may be affected, chiefly the joints of the extremities, but also the joints of the jaws and spinal column have been attacked. The skin over the joints does not turn red or warm, but there is a strong swelling. When the finger joints are affected, there is thus no space between the fingers. At times there may be swelling of the regional lymph glands. Between the attacks the patient is quite free from joint symptoms of any kind.

Simultaneously with or independently of the joint symptoms there may occur rapidly arising, transitory eruptions of the skin, consisting of red, as a rule slightly elevated papulae with dentate edges. The skin eruptions are not accompanied by any rise in temperature.

The patient has always been sensitive to cold and thinks it may bring on attacks if she gets cold. Only a few times, however, have there been cold shivers without apparent reason, the patient not being at the time in cold places. Under such circumstances there has on rare occasions been a rise in temperature to 38°-39°. Has never noticed dark urine in connection with the cold shivers. All through her life there has been a certain tendency to anemia.

After this brief survey, the patient's affection will be described from discharge cards and case records.

In 1939, at the age of 11, she was for about 10 days in the Medical Department of Aarhus District Hospital. The diagnoses were Quincke's edema, urticaria. Transitory hyperemic spots were observed in the face and on the arms. Hemoglobin 85 p.c. In 48 hours Mantoux was + + +. In the asthma-cutaneous tests there was a slight positive reaction to albumen, veal, and horse meat. During her stay she had a paradysentery (Sonne).

At the age of 14 admitted to Department P, the Rigshospital. Diagnoses: Edema Quincke, urticaria, periodontitis, leucocytosis, increased sedimentation. Of the laboratory tests it may be noted that the hemoglobin percentage was 75. The sedimentation rate between 68-96 mm. The leucocyte values were between 18,000 and 42,260 (with normal differential count, especially no eosinophilia). The anti-streptolysin titre was 130. Widal negative. A hyperglobulinemia was demonstrated, the total protein being 9.15 p.c., albumin 4.41 p.c., and globulin 4.74 p.c. Cutaneous tests for allergy were without sure positive reactions. Treatment (ut aliquid fiat): Extraction of 4 + and + 5. As the positive reactions were uncertain, desensibilisation was performed with veal and albumen.

In an ambulant examination at the age of 17 by Chief Physician Dalsgaard-Nielsen the case was regarded as an allergosis. Further she showed symptoms of a labile, vegetative nervous system, manifesting itself by unconsciousness during the sinus-caroticus reflex. In addition there was a slight transitory iridocyclitic and a slight paling of the papillae.

In 1947, when she was 19, she was for a couple of months in the Rigshospital, Department B, the diagnosis being hyperglobulinemia. The serum protein was 9.53 and 8.63 p.c. with albumin values of 3.74 and 3.86 respectively and globulin values

of 5.79 and 4.77 p.c. The sedimentation rate was between 96 and 151 mm. Hemoglobin percentage 76-77. Index 1.06. Leucocytes 11,300, differential count normal. Mantoux I: +. Skin biopsy: no certain pathological changes. Lymph gland biopsy: edema and slight plasma cell infiltration. Special dermatological examination: urticarial erythema, presumably of an allergic character. Antistreptolysin titre 100. Examination of the eyes: obs. for incipient atrophy of optical nerve. Slight double-sided conjunctivitis. X-ray examination of heart, lungs, both hands, the skull, the right upper arm, the femur, column and pelvis showed nothing abnormal. Electrocardiogram normal.

From January to March 1948 the patient was at the Neurological Department of Frederiksberg Hospital. During her stay here she was for a time transferred to Medical Department E for examination. Our diagnosis was allergosis ?, that of the Medical Department hyperglobulinemia, Observatio.

At Christmas time there had for a time been uncharacteristic dyspeptic trouble with distaste for food, loss of weight, and a burning pain in the epigastrium, without relation to meals or relief after eating.

The reason for admission was an examination with a view to a possible streptomycin treatment.

Upon admission and during the stay there were eruptions of rather transitory urticaria-like skin affections. No visible icterus. No swelling of the liver, spleen or lymph glands.

The neurological findings were a slight facies oleosa, and the facial movement was perhaps rather slight. Speech rather slow, no dysarthria. The left abdominal reflex somewhat greater than the right, on the left side of the trunk the patient stated there was slight hyperesthesia. The clinical neurological examination showed nothing abnormal, especially no Babinski.

Upon admission the examination of the eyes and the ophthalmoscopy showed normal conditions. During the stay there came a right-sided iridocyclitis and the right papilla became pale and poor in vessels, so that the oculists at one time reckoned with atrophy of the optic nerve. A couple of weeks later there was still a somewhat pale right papilla, though it could not with certainty be called pathological, and the iridocyclitis had subsided.

The total serum protein was 9.0 p.c., albumin 4.4 p.c. and globulin 4.6 p.c. Hemoglobin (Sicca) was between 72 and 77 p.c. Erythrocyte values between 3.59 and 3.94 millions. Colour index between 0.96 and 0.88. Differential count showed normal conditions, especially no eosinophilia. Blood platelets 498,000. Number of white blood cells between 12,488 and 24,400. Sedimentation rate between 47 and 91 mm. As the blood cells did not sediment with a sharp limit, a determination was made of the osmotic resistance of the red blood cells and a reticulocyte count which showed normal values.

By a differential count of the peripheral blood and by bone marrow puncture, performed by Prosector Søbørg Ohlsen, no unripe cell forms were found in the peripheral blood, but a fairly marked shifting to the left. The marrow punctate rich in cells showed a hyperplastic, myelocyte system with displacement to the left comprising the neutrophilous myelocytes. The number of plasma cells was increased (1.25 p.c.). The findings were stated to correspond to a toxic infectious state with complicating slight microcyte anemia. In a telephone talk with the prosector it was confirmed that the plasma cell number must be regarded as absolutely increased, when the hyperglobulinemia is taken into account.

The cerebro-spinal fluid showed a pressure of 420/240 with rise and fall upon

Queckenstedt's test and using the abdominal press. 13/3 leucocytes + 2/3 lymphocytes. Albumin value 30-35, globulin value 3-4 (a.m. Bisgaard).

X-ray examination of the cranium, teeth, and ossa temporalia showed natural conditions, apart from a sinusitis maxillaris et ethmoidalis duplex. A special examination at the Ear Department revealed no clinical symptoms of sinusitis. X-ray of the column and pelvis: halisteresis. X-ray of left knee: nothing abnormal.

Electrocardiogram normal. Venyle blood and blood cultures gave no growth. Antistreptolysin titre between 40 and 65. No agglutination titre. Widal negative. α -staphylococantitoxin titre was 10 units per cc of serum, i.e. increased. Kveim's reaction for Boeck's sarcoid negative.

After her discharge she had the usual joint and skin affections, but on the whole felt well. She could do her work as a photographer's pupil, and in addition, as so often before, was occupied with the training of horses. During this work she fell off a horse and hurt her back. A chiropractor observed the obligatory displacement of the vertebrae, which, however, he could not treat till the patient had been admitted to hospital and subjected to a "shock treatment".

In November 1948 she was at the Neurological Department of Aarhus Municipal Hospital with the diagnosis Obs. pro Morbus Bing-Neel. The last months before admission there were intermittent symptoms from the central nervous system in the form of subjective disturbances in sensation and paresthesias of the right upper extremity and the left side of the face. In addition periodical difficulty in controlling the right-sided extremities and a feeling of paresis of the same. The last week before admission tremor and dyspraxia of the right hand, and difficulty in controlling both legs. Now and then there had been double sight.

Objectively she seemed in a psychic respect a little infantile. Passed inculcation and concentration tests well. Neurological examination again showed that the abdominal reflex on the left side was livelier than on the right, but on the whole both were slight. In the upper extremities there was right-sided tremor, dysdiadokokinesia and slight deep reflex predominance with Hoffmann's sign. In the lower extremities slight double-sided paresis, some spastic increase of tone, double-sided Babinski, but rather slight deep reflexes. Marked ataxia at the knee-heel test and gait, which was only possible with support.

Examination of the eyes: Some hyperemia of the conjunctiva of the right eye, nystagmus on glancing to the right and a slight diffuse paling of the papillae on both sides.

Cerebro-spinal fluid 37/3 cells, albumin 42, globulin 4. (Dilution-method).

The Laboratory tests corresponded to the earlier findings. The hemoglobin percentage was 75. Number of white blood cells 15,700. Sedimentation rate between 85 and 90 mm. Formolgel reaction positive in three hours. A fresh sternal puncture showed active bone marrow with dominant granulopoiesis and a slight increase of plasma cells. During the stay a great eruption of quite typical urticaria (Professor Lomholt).

Discharged considerably improved, there was, however, still double-sided Babinski, difference in the abdominal reflexes and sprawling gait with lurching on turning.

On December 31, 48, the patient was again admitted to Frederiksberg Hospital, Neurological Department. In the time that had elapsed the condition had been variable. Now and again there had been powerlessness and pain in the arms and legs. The gait had periodically been lurching. It was stated that there had not been fever.

Upon admission she seemed objectively much reduced in a psychic respect. Questions are answered carelessly, she follows up her own thoughts, and is difficult to interrupt or divert. Is rather loquacious, mostly fabling about the chiropractor, Aarhus Municipal Hospital, and her fall from the horse. Also as a whole rather refractory, especially with regard to her toilet.

There are transitory eruptions of the skin disease.

Face movement very slight, face perspiring, a little oily.

Papillae a little pale temporally, especially on the right side, though this cannot be said to be pathological. Slight nystagmus upon extreme side glances. Speech lisping, nasal, perhaps slightly bulbar in character, and slower than usual. No paresis of the velum. The tongue is put out straight. The patient can only swallow liquid food.

In the upper extremities the power is slight. There is a moderate predominance of the right-sided tendon reflexes. With a fit of coughing there is coarse tremor of the right hand. Finger-nose tests inaccurate, possibly because of lack of co-operation. The diadokokinesia on both sides slow and groping, probably for the same reason.

The abdominal reflexes lacking on the right side, slight on the the left.

The lower extremities: Cannot move the left leg on account of pain from joint affections in the hip. No swelling or glandular tumour. The tendon reflexes on the right side livelier than on the left. There is double-sided Babinski and Oppenheim.

The statements concerning sensibility vary, as a rule there seems to be most sensibility in the right half of the body and the right leg.

Dermographism develops slowly but distinctly with swelling along the scratches and erythema in a zone about 4 cm broad.

In the course of about ten days the speech becomes less nasal, and she can swallow solid food. The pareses and the joint affections subside. The psychic symptoms disappear and she returns to her habitual slightly infantile state. The face remains salve-like with reduced facial movement. There are still periodical transitory erythemas and for a time joint symptoms from the right elbow. The changes in the abdominal reflexes and the reflexes of the lower extremities can still be seen. She can manage to eat and can soon walk with the aid of two sticks.

During the last stay the sedimentation was between 135 and 112 mm. The same blood sample shows a sedimentation reaction of 105 and 136 mm. respectively at room temperature and at 37°. Formolgel reaction positive after half an hour. Blood percentage (Sicca) about 70. Erythrocytes 3.18 mill. Index 1.04. White blood cells 17,600.

The urine has for the first time during the hospital stays contained albumin, ranging between 0.1-0-0.05. Urine microscopy showed nothing abnormal. Bence-Jones protein negative. Urine culture gives growth of Gram-negative, not lactose-fermenting rods and Gram-positive diplococci.

Serum protein 11.1 p.c., albumin 4.8, globulin 6.3 p.c.

Pressure of cerebro-spinal fluid 300/60 (for therapeutic reasons 30 cc were drawn). Cells 0/3, albumin 13-14, globulin 2-3 (a striking difference in the values compared with the figures from Aarhus Municipal Hospital a couple of months earlier, though the patient has also now acute cerebrospinal symptoms). No growth on culture from the spinal fluid, nor does direct microscopy show any bacteria.

The α -staphylococantitoxin titre is this time 4 units, i.e. of dubious increase. Normal antistreptolysin titre and cold-agglutinin.

Serum phosphatase, acid phosphatases, icterus index, takata, and thymol reaction showed normal values.

Prausnik-Küster's reaction negative for horsehair.

The electrocardiogram for the first time showed deviations in the form of negative T₂ T and T₃.

X-ray examination of lungs, skull, paranasal sinuses, pelvis, left femur, right crus, and the spinal column presented nothing new.

Serum calcium and phosphorus slightly raised with values of 12.2 and 5.5 p.c., respectively.

For the sake of completeness it may be mentioned that the Wassermann reaction was always negative, both in the blood and the spinal fluid. Blood pressure and temperature conditions were also normal during the many hospitalisations.

DISCUSSION

The very detailed history shows that futile attempts have been made to find grounds for myelomatosis.

Lupus erythematoses disseminatus can no doubt be disregarded, inter alia because there have been no febrile periods or gastro-intestinal disturbances during the acute attacks. In addition leucopenia and thrombopenia might be expected.

Even through no reddening of the joints is seen during the acute attacks the clinical examination suggests Palindromic rheumatism (*Hench & Rosenberg 1944*). The non-febrile course and the fact that the X-ray showed no changes of the joints after the affection had persisted for so many years may lend support to that assumption. The moderate protracted anemia, the fairly marked leucocytosis, the hyperglobulinemia, and now finally the symptoms from the central nervous system, do not, however, come under the concept of Palindromic rheumatism.

The history and the examination afford no grounds for rheumatic fever. In connection with the other clinical results, therefore, proliferative, endarteritic processes, as described by *Bruetsch (1944)*, may no doubt be disregarded.

Hyperglobulinemia essentialis (*Waldenström, 1944*) has been found in much older patients with a more pronounced anemia and a tendency to bleeding. The leucocyte values are not so high, and there are no cerebral symptoms, nor are there the above-mentioned skin and joint affections.

The clinical picture may in the last months present certain points of resemblance to morbus *Bing-Neel (1936)* and the case later described in collaboration with *Fog (1937)*. The long history with the

allergically marked manifestations from the skin and joints are peculiar to my patient, just as there have been no subfebrile conditions or signs of more acute infections.

SUMMARY & CONCLUSION

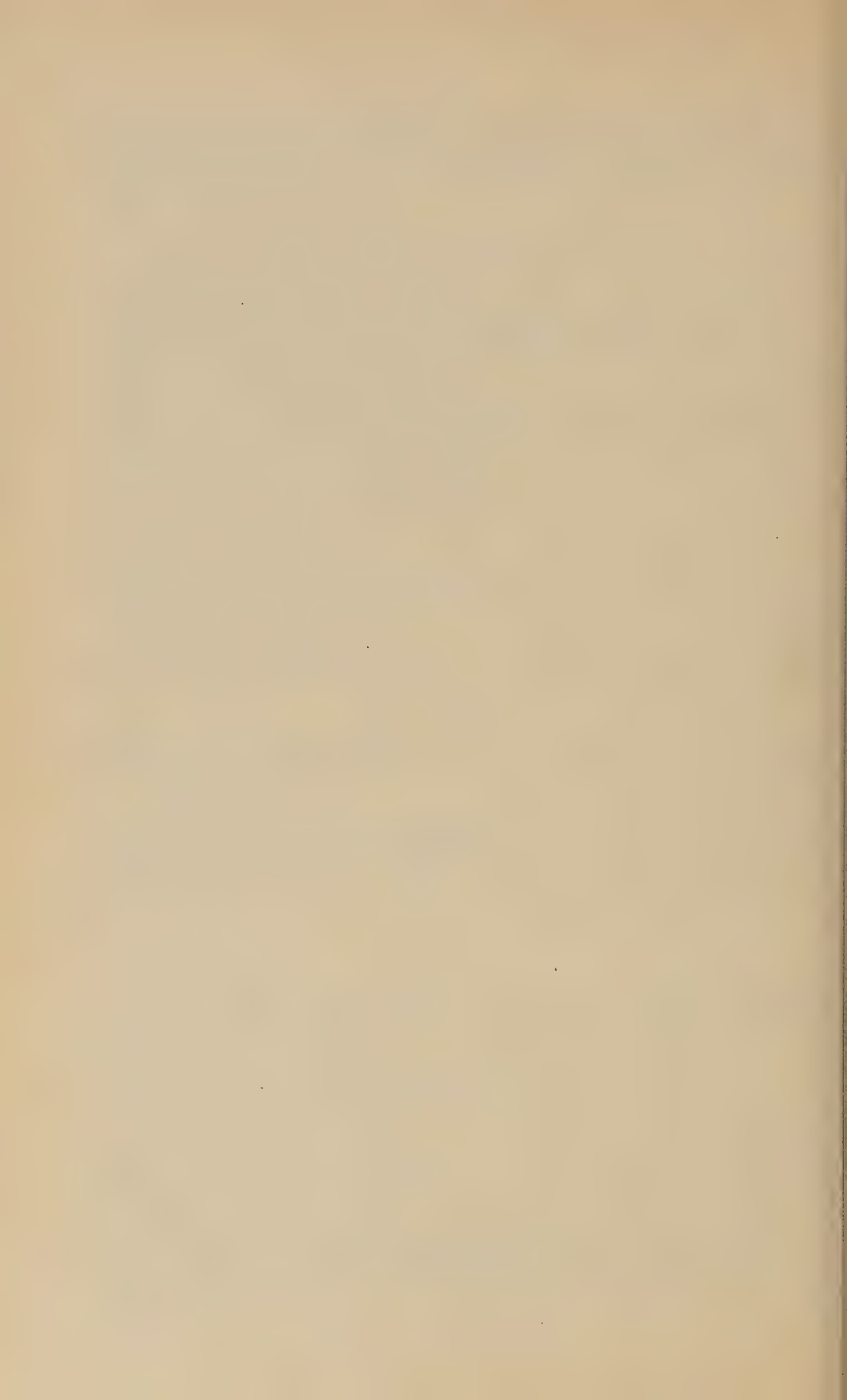
The patient is a woman, aged 20, who since the age of five has presented clinically acute, allergically marked manifestations from the skin and joints. The last few years there have been rather transitory eye symptoms (iridocyclitis and changes of the papillae) as well as fluctuating radicular and cerebro-spinal manifestations which allow of no focal diagnosis. There has always been a tendency to a moderate anemia and since the age of 14 the findings in the repeated hospitalisations have constantly been leucocytosis, hypersedimentation, and hyperglobulinemia, findings which in connection with the later examinations of the bone marrow must be put down to an infectious condition. No certain indications of the seat or nature of a non-febrile infection could be gained, since there was only a positive Mantoux and a transitory α -staphylococantitoxin titre to go by. The last year there have also been observed changes of a somewhat fluctuating character in the cerebro-spinal fluid.

The clinical picture at the bedside, during the acute phases, seems more allergic than toxi-infectious. It has not, however, been possible to demonstrate supersensitiveness to the usual allergenes, particularly horsehair. The absence of eosinophilia does not exclude allergia. To explain the syndrome, it is presumably not possible entirely to disregard an allergic mechanism, produced by proteins originating from an infectious focus.

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DIE WIRKUNG
DER HYPOGLYKÄMIEBEHANDLUNG AUF DAS HERZ,
NACH BEFUNDEN DES
ELEKTROKARDIOGRAMMS (EKG)

Von

ERWIN HASCHÉ

Schon bei Beginn der Insulinbehandlung der Psychosen an hiesigem Krankenhaus durch J. Agerberg — 1935 — wurde erkannt, dass das wichtigste Risiko dieser Behandlung in der Gefahr der Ueberdosierung liegt, weil die Shockdosis bei den einzelnen Patienten im Verhältnis ca. 1:20 schwankt und auch bei demselben Patienten im Lauf der Zeit sich um ein Vielfaches ändern kann. Es wurde an hiesigem Krankenhaus daher auf eine sorgfältige und vorsichtige Dosierung von Anfang an Wert gelegt und dieses Sicherheitsprinzip hat sich bewährt: in den vergangenen 15 Jahren ereignete sich in Gegensatz zu anderen Anstalten an hiesigem Krankenhaus kein einziger Todesfall in Zusammenhang mit der Insulinbehandlung. Nur vereinzelt traten Komplikation in Form von Weckschwierigkeiten auf, schwerere Fälle in Verbindung mit Kollaps nur 5 in 15 Jahren.

Um festzustellen, welche Faktoren bei dieser Dosierungsart eine Rolle spielen, wurde im folgenden der klinische Zustand derjenigen Kranken einer genaueren Analyse unterzogen, die unter der Insulinbehandlung Zeichen stärkerer Allgemeinwirkung zeigten wie langfristig erhöhter Puls, Extrasystolen, Arythmien, Blutdruckschwankungen, Kollapsneigung, Cyanosen, unbegründete Temperatursteigerungen oder Untertemperaturen. Da das häufigste klinische Symptom eine kontinuierliche, langdauernde Pulserhöhung ist, die oft in keinen Verhältnis zu stehen scheint zur Dauer und Stärke des angewendeten Insulins, befasst sich diese Studie hauptsächlich mit dem Herz sowie mit dem Ekg als objektivem Registrierverfahren.

Übersichtshalber werden die Behandlungen in „Schwach“- und „Stark“-behandlungen eingeteilt, wobei die Grenze zwischen beiden Behandlungsarten durch

den Grad des Bewusstseinsverlustes unter der Behandlung bestimmt wird: solange die Patienten die Zuckerlösung selbst trinken können und hinterher genaue Erinnerung haben, wieviel Glas sie getrunken haben, rechnet die Behandlung zur „Schwachbehandlung“, alles übrige zur „Starkbehandlung“. Die Schwachbehandlung wird täglich am Vormittag 4-5 Stunden durchgeführt, die Starkbehandlung je nach der Stärke der klinischen Wirkung, die wie folgt angezeigt wird:

- (+) = partielle Amnesie. Trinkfähigkeit vorhanden, aber hinterher keine klare Vorstellung, wieviel Glas getrunken worden sind. Behandlungszeit: 4—5 Stunden.
- + = volle Amnesie. Trinkfähigkeit vorhanden, aber hinterher keine Erinnerung, dass getrunken worden ist. Behandlungszeit: 4—5 Stunden.
- ×...× = Halbchock. Keine Trinkfähigkeit, aber direkte oder reflektorische Ansprechbarkeit noch vorhanden. Behandlungszeit: höchst 1 Stunde nach Eintritt des Halbchock.
- |—| = Vollchock. Keine Ansprechbarkeit. Behandlungsdauer $\frac{1}{2}$ Stunde nach Eintritt des Vollchock.

Die Ekg-Aufnahme erfolgte, abgesehen von besonders angegebenen Ausnahmen, am Nachmittag, 2—4 Stunden nach abgeschlossener Behandlung. Die Registrierungsergebnisse werden nach den drei Hauptgruppen des Ekg, Vorhof, Ventrikel und Coronarien, mitgeteilt. Nomenklatur nach (1). Kein Patient erhielt Medikamente, keiner hatte Fieber. F ist die Herzfrequenz. Als Mass für den Rythmus findet sich hinter F eine Zahl mit $\pm$ -Zeichen, die die grössten Abweichungen der Frequenz vom Mittelwert derselben angibt, der sich aus der Registrierung ergibt. Die „Beurteilung“ des Ekg-Befundes erfolgte nach den z. Z. gültigen Regeln (siehe 1). Nur Abweichungen vom Normalen sind angegeben. ♀ = Frauen, die übrigen sind Männer.

- 0 = klinisch unbedeutender Befund
- + = klinisch beachtenswerter Befund
- ++ = sicher pathologischer Befund.

1. Erstmalige Schwachbehandlung.

Fall. Nr.	Vorhof	Ventrikel	Coronarien	Beurteilung
3	—	Q ₃ positiv	—	+
4	P ₁₋₃ gesplittert F = 91 ± 3	atypischer Wilson- block (ohne Q ₃)	—	++
8 ♀	P ₁ gesplittert P ₃ unregelmässig	—	—	+
11	F = 101 ± 1	atypischer Wilson- block	—	++
13	P _{2,3} > 0,1" F = 86 ± 10	—	—	+
16	P _{2,3} gesplittert PQ = 0,22" F = 62 ± 11	—	—	+
27	P ₁ = 0. F = 91 ± 3	Extrasystolen, Wilsonblock	—	++
61	PQ = 0,18" F = 86 ± 2	Q ₁ positiv	T ₁ = 0	++
67	P ₁₋₃ gesplittert Aurikuläre Extrasystolen F = 101 ± 2	0,7 mV	—	+
70 ♀	P ₂ = 0 P ₃ unregelmässig und gesplittert F = 73 ± 16	Niedrige Voltzahl (0,4 mV)	—	++
73 ♀	P ₁ = 0. P ₂ > 0,1" P ₃ gesplittert F = 98 ± 7	—	—	+
83 ♀	F = 97 ± 2	0,4 mV. S _{2,3} pos. partiell Wilsonblock	—	+
85 ♀	Aurikuläre Extrasystolen, P ₂ diphasisch P ₃ fast 0 F = 103 ± 8	—	(ST) ₁ gesenkt T ₁ = 0 T ₂ fast 0. T ₃ negativ (ST) ₂ gesenkt	++ +

Ausserdem 7 Fälle ohne EKG-Befund.

2. Wiederholte Schwachbehandlung.

Fall Nr.	Vorhof	Ventrikel	Coronarien	Beurteilung
7 ♀	P ₂ gesplittert P ₃ = 0	—	—	+

Ausserdem 2 Fälle ohne Befund.

3. *Erstmalige Starkbehandlung.*

Fall Nr.	Vorhof	Ventrikel	Coronarien	Beurteilung
6 ♀	$F = 77 \pm 8$	geringe Voltzahl (0,7 mV)	—	+
15	$F = 133 \pm 1$ P ₁ gesplittert			
	P _{2,3} gross	—	T ₂ negativ	+
20 ♀	P ₁ = 0 P ₂ gesplittert	—	T ₁ = 0. T _{2,3} negativ (ST) ₂ gesenkt	+
25	Aurikuläre Extrasystolen	—	—	0
21 ♀	P _{1,3} diphasisch u. gesplittert P ₁ neg. P ₂ gross $F = 90 \pm 2$	—	—	+
30 ♀	P ₁ gross. P ₂ gesplittert. P ₃ neg. $F = 83 \pm 3$	Q ₃ positiv	—	++
32 ♀	P ₂ gross PQ = 0,2"	—	—	+
	$F = 92 \pm 3$			
33	$F = 77 \pm 8$	—	T ₂ diphasisch u. klein	0
34 ♀	$F = 120 \pm 2$	0,5 mV	—	+
35 ♀	P ₃ gesplittert $F = 106 \pm 8$	—	—	0
38 ♀	$F = 94 \pm 3$	—	T ₃ negativ (ST) ₃ gesenkt	0
41	$F = 112 \pm 8$	—	T ₃ negativ	0
80	PQ = 0,2"	S _{1,2} breit	—	+

Ausserdem 16 Fälle ohne EKG-Befund.

4. Wiederholte Starkbehandlung und kombinierte oder wiederholte Schwach- und Starkbehandlung.

Fall Nr.	Vorhof	Ventrikel	Coronarien	Beurteilung
9	P _{1,2} klein. P ₂ hoch u. $> 0,1''$. PQ = $0,2''$ F = 103 ± 8	—	T ₂ fast 0	+
14	F = 86 ± 2	0,7 mV	—	0
51	F = 80 ± 6 P ₃ negativ	S _{2,3} stark pos. 0,6 mV	—	++
37 ♀	F = 85 ± 9 P ₃ fast 0	—	T ₃ negativ	0
52	P ₂ gesplittert P ₃ negativ und gesplittert	—	—	0
54	F = 83 ± 2	S ₂ breit, 0,6 mV	—	+
55	F = 106 ± 9	0,7 mV	—	+
56	F = 63 ± 12 PQ = $0,2''$	—	—	0
59	F = 123 ± 5 P ₁ diphasisch	—	—	0
64	linksseitiger Wilsonblock (atypisch)	—	—	++

Ausserdem 6 Fälle ohne EKG-Befund.

Anmerkung: Sämtliche Patienten fieberfrei z. Z. der Ekg-Aufnahme, und haben normalen Blutzucker.

Im ganzen kamen 69 Patienten elektrokardiographisch zur Untersuchung, welche sämtlich gegenüber Hypoglykämie klinisch eine gewisse Labilität hinsichtlich Kreislauf und Herztätigkeit zeigten. Von diesen Kranken hatten fast die *Hälfte* (31) *keinen* Ekg-Befund. Von den übrigen 38 ist folgendes zu sagen:

Auffallenderweise zeigt die erste Gruppe (erstmalige Schwachbehandlung) die *grössten* Störungen, während Starkbehandlung und wiederholte Behandlung kleinere Störungen zeigen. Das steht in Uebereinstimmung mit der klinische Beobachtung, nach der die gegenüber Hypoglykämie labilen Patienten durch geeignet geführte Behandlung *so trainiert* werden können, dass die Insuffizienzerscheinungen verschwinden.

Coronarinsuffizienz trat nie auf. Geringfügige andersartige Veränderungen an den Coronarien: 7 Fälle (Änderungen in T₃ nicht mitgerechnet).

Herzmuskelbeeinflussung: positives Q₃: 2 Fälle. Niedrige mV-Zahl: 8 Fälle. Kombination beider Symptome: kein Fall.

Kombinierte Ventrikel + Coronarveränderung: 1 Fall.

Der *Hauptteil* der Veränderungen betrifft den *Vorhof*: 21 Fälle mit P = Änderungen, 6 Fälle mit Verlängerung der Ueberleitungszeit, 20 Fälle mit Tachykardie, 14 Fälle mit Arythmie, 3 Fälle mit aurikulären Extrasystolen, 2 Fälle mit Aufhebung der Synchronität beider Ventrikel (Wilsonblock), 6 Fälle mit Vorstufen dazu (breites S).

Das Ueberwiegen der Veränderungen bei den *Männern* ist bemerkenswert:

Ekg-Störungen	Anzahl	Patienten
	♂	♀
0	7	3
+	10	9
++	6	3
Summe:	23	15

3 Kollapse kamen elektrokardiographisch zur Untersuchung, sämtlich *Männer* betreffend:

1) Fall Nr. 42, geb. 1921. Kollaps bei 136 i.E.¹, kein Chock. Ekg nach 1 Tag: F = 78 ± 3 , sonst 0. Nach 2 Monaten: F = 49 ± 2 , nach 1½ Jahr: F = 58 ± 2 , also *vollständig* 0.

2) Fall Nr. 15, geb. 1917. Nach 8 halbstündigen „normalen“ Vollchocks, sowie vorangehender Schwachbehandlung von 5 Monaten „plötzlicher“ Kollaps. S. Tabelle, Abschnitt 3: Zustand 2½ Stunden nach Einsetzen des Kollapses. Ein Tag darauf: F = 95 ± 1 , sonst 0. Dieser Patient hatte schon vor Behandlungsbeginn einen ausgeprägten klinischen Befund: verbreiteter Iktus 1 cm ausserhalb der Mamillarlinie, 2. P. T. acc, systol. Blaston, Blutdruck: 175/65, Ekg: P_s negativ, F = 100 ± 17 . Chockdosis: 152 i.E.

3) Fall Nr. 51, geb. 1881. Hatte vor Beginn der Behandlung eine Bradykardie von 38, welche unter schwachen Insulindosen langsam auf F = 80 ± 10 ansteigt. Ein Ekg in dieser Zeit lautete: P_{2,3} gesplittet, S_{2,3} stark positiv, F = 61 ± 2 , maximale Spannung 0.45 mV. Im Laufe eines Monats Starkbehandlung mit langsam steigenden Dosen bis 328 i. E., ohne dass hypoglykämischer Chock eintrat. Statt dessen plötzlich Kollaps mit Vorhofsfimmern, F = 136 ± 50 . In obiger Tabelle, Abschnitt 4, Zustand nach 9 Monaten und inzwischen erneut durchgeführter Insulin-Schwachbehandlung: wesentliche Änderungen im Ekg gegenüber früher sind *nicht* vorhanden.

¹ i. E. = internationale Insulin-Einheiten.

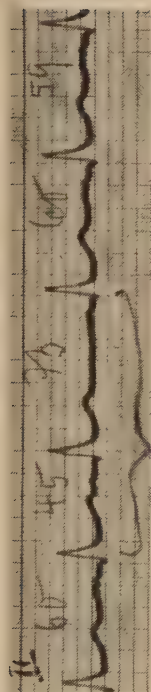


Bild 1.
Fall 67, Abl. 2
♂ 67 Jahr

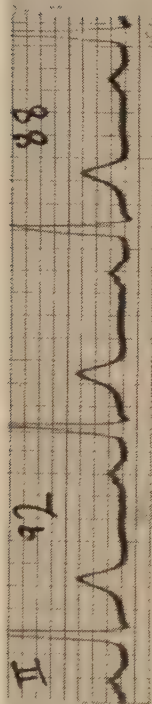


Bild 2.
Fall 16, Abl. 2
♂ 34 Jahr

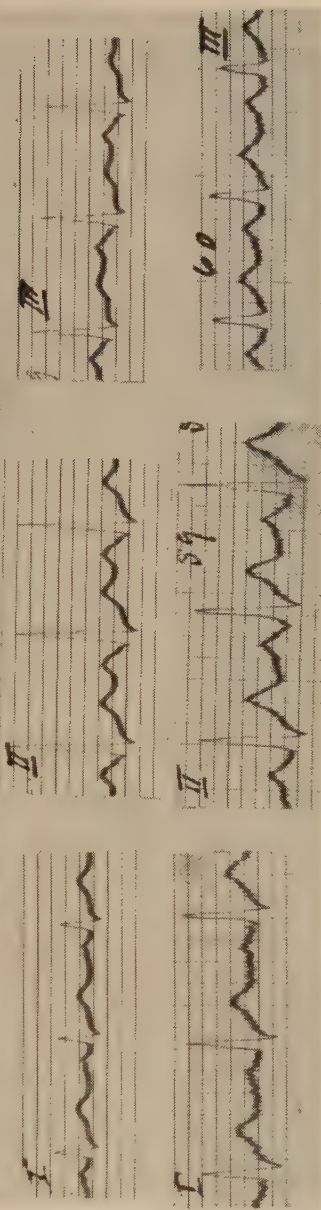


Bild 3.
Fall 59
♂ 45 Jahr

Bild 4 a.
Fall 11
♂ 27 Jahr

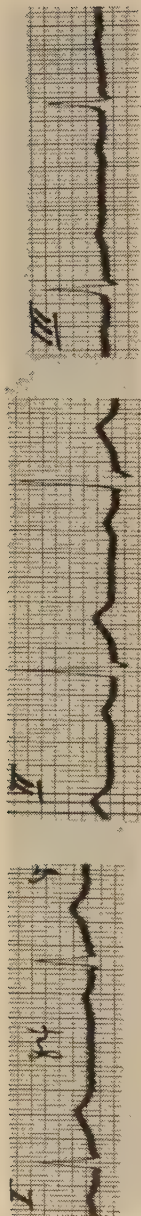


Bild 4 b.
Fall 11

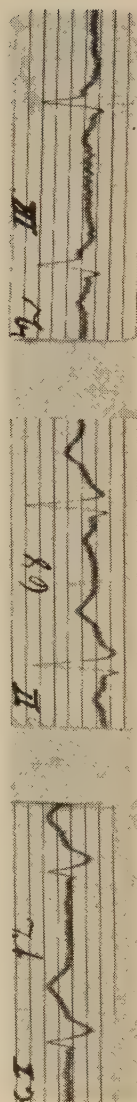


Bild 5.
Fall 64
♂ 26 Jahr

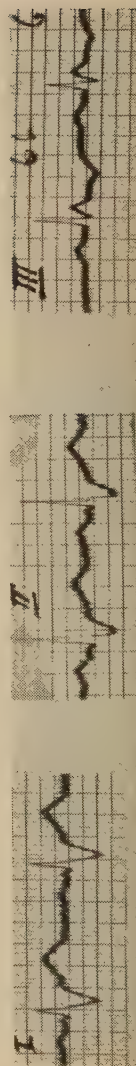


Bild 6.
Fall 27
♂ 68 Jahr

Abb. 1.

Ekg-Änderungen durch Insulin, 2-4h nach Zuckergabe, 7-9h nach Insulingabe (Nur abweichungen vom Normalbild werden angegeben); Rektaltemperaturen, normaler Blutzucker).

Bild 1. Aurikuläre Extrasystolen. Mehrphasiges und flaches P in allen Ableitungen. Niedrige mV-Zahl (0,7 mV max). Tachykardie ($F = 101 \pm 2$ bei $t = 36,7^\circ \text{C}$). 48 i. E.

Bild 2. Mehrphasiges P_{2, 3}, grösser als 0,1" (max: 0,12"). Verlängerte Ueberleitungszeit (max: 0,22"). Arythmie ($F = 62 \pm 11$ bei $t = 36,9^\circ \text{C}$). 12 i. E.

Bild 3. Tachykardie bei normaler mV-Zahl. (Dies Beispiel ist hauptsächlich für den Vergleich des S-Stückes und des verbreiterten QRS-Stückes mit den folgenden Bildern hier angeführt). $F = 123 \pm 5$ bei $t = 37,2^\circ \text{C}$. P₁ diphasisch. 80 i. E.

Bild 4-6. Intraventrikuläre Leitungsstörungen.

Bild 4 a. Bei Insulin-Sensibilisierung. Grosses P₂. Verbreitertes QRS. S breit in allen Ableitungen, keine isoelektrische Linie zwischen S und T. Tachykardie ($F = 101 \pm 1$ bei $t = 37,3^\circ \text{C}$). Niedrige mV-Zahl (0,7 mV max). 52 i. E.

Bild 4 b. Nach Insulintraining. Bis auf eine — konstitutionell bedingte — Arythmie in allen Teilen normalisiertes Ekg. $F = 76 \pm 11$ bei $t = 37,9^\circ \text{C}$. mV max = 1,4. — 112 i. E.

Bild 5. Breites S₁ ohne nachfolgende isoelektrische Linie. S₂ ohne nachfolgende isoelektrische Linie. P₁ = 0. Q₃ an der Grenze des Normalen. Tachykardie und Arythmie ($F = 83 \pm 8$ bei $t = 37,1^\circ \text{C}$). 56 i. E.

Bild 6. P klein in allen Ableitungen. Breites S_{1, 2}, fast ohne isoelektrische Linie vor T. Ausgeprägtes S₃ mit positiver Nachschwingung. Tachykardie ($F = 91 \pm 3$ bei $t = 37,2^\circ \text{C}$). 20 i. E.

Zusammenfassend ist zu sagen, dass das Ekg in keinem Fall, selbst nicht nach langfristig durchgeführter Starkbehandlung und auch nicht im und nach Kollaps organische Herzveränderungen zeigt. Die Hauptänderungen sind funktioneller Natur, die bei den 3 schweren Zwischenfällen ausserdem *reversibel* waren.

Dies Ergebnis legt die Untersuchung nahe, ob Reversibilität auch in den übrigen Fällen vorliegt und die Störungen durch *entsprechende Dosierung* vermieden werden können, sodass also die im Ekg angegebenen funktionellen Herzstörungen als *Zeichen von Insulinüberdosierung* gedeutet werden können, worauf der in den Tabellen ange deutete „Training“-effekt bereits hinweist. Unsere Versuche ergaben:

Wenn man für einen ruhigen, nicht durch Agitation und klonische Krämpfe gestörten Chockverlauf sorgt, kann man tatsächlich durch Reduktion von Insulinmenge oder-zeit die Ekg-Symptome zum Verschwinden bringen. Weiterhin sieht man, dass in diesem Fall die Insulindosis, falls noch keine Chockwirkung vorliegt, jeden zweiten Tag um ca 8 i. E. erhöht werden kann, ohne dass neue Ekg-Symptome auftreten. Treten neue auf, genügt ein Aufenthalt in der Dosiserhöhung für einige Tage, um dieselben zum Verschwinden zu bringen

(*Training*). Von den auf diese Weise behandelten Patienten zeigten am Schluss nur noch 7 Patienten (= 10 %) *geringfügige* Form = und Grösßenänderungen einer oder zweier P-Zacken. Diese finden sich aber auch im Kontrollmaterial und bei Gesunden und können nicht als pathologisch angesprochen werden.

Praktisch wichtig ist, dass sich für eine solche Dosisführung genügend *klinische* Zeichen finden lassen, die man *anstelle* des Ekg benutzen kann, wodurch man von diesem *unabhängig* wird. Hiervon sei genannt:

1) Die *Sensibilisierung* für Insulin tritt bei der vorliegenden „Trainingsbehandlung“ im Gegensatz zur Dosierung ohne Training und mit stark steigenden Dosen nach erreichten Chockdosen ziemlich *schnell* ein. Man muss daher schon nach 1 Woche täglicher Chocks die Dosis senken, um nach Sensibilisierung zu fahnden. Wir senken in diesen Fall täglich um 8—16 i. E. und können oft die Dosis bis zu 30—50 i. E. senken, ohne dass sich am Chockverlauf etwas ändert. Auf diese Weise wird eine erhebliche, bereits eingetretene Sensibilisierung rechtzeitig beseitigt: „stille“ oder nach v. Braunmühl (4) „latente“ Sensibilisierung, da sie ohne ein klinisches Symptom erfolgt. Treten erst Symptome auf, so ist hohe Gefahr im Anzug. Denn die schon vorhandene „stille“ Sensibilisierung kann sich dann lavinenartig verstärken und der Patient kommt „plötzlich“ in schweren Kollaps, aus dem er nur mit Mühe herausgeholt werden kann. Solche Symptome sind: Mattheit und Unlust nach der Behandlung, Appetitlosigkeit, Brechneigung oder Erbrechen, sofern dieses nicht mechanische Ursache hat (Ueberfüllung des Magens mit Magensaft oder Galle). In diesen Fällen ist sorgfältige Magenspülung und = Entleerung vor der Zuckergabe wesentlich sowie zur Vermeidung grossen Volumens möglichste Konzentrierung des Zuckers. Oft ist das einzige Symptom einer beginnenden Dekompensierung die positive Ehrlichsche Urobilinogenreaktion im Harn (mit Paradimethylamidobenzaldehyd). Auch hier ist Dosissenkung zu empfehlen sowie zu „trainieren“, bis die täglich auszuführende Ehrlich-Reaktion Null ist. Dann erst wieder langsame Steigerung hinsichtlich Insulinzeit und danach auch Insulindosis, falls Ehrlich Null bleibt.

2) *regelmässige Anzeichnung* der Zeit, zu der der Patient in „Halbchock“ kommt, die nach Braunmühl gerechnet wird vom Augenblick, wo der Schluckreflex verschwindet. Viele Patienten kommen früh in „Halbchock“ und spät oder garnicht in Vollchock. Wenn man den „Halbchock“ nicht anzeichnet, so sieht es bei diesen Patienten aus, als hätte „keine Wirkung“ oder nur eine „unbedeutende“ vorgelegen. Es hat sich aber gezeigt, dass für den „Halbchock“ dieselben Regeln

Kurve S. 2

Name: N. N.

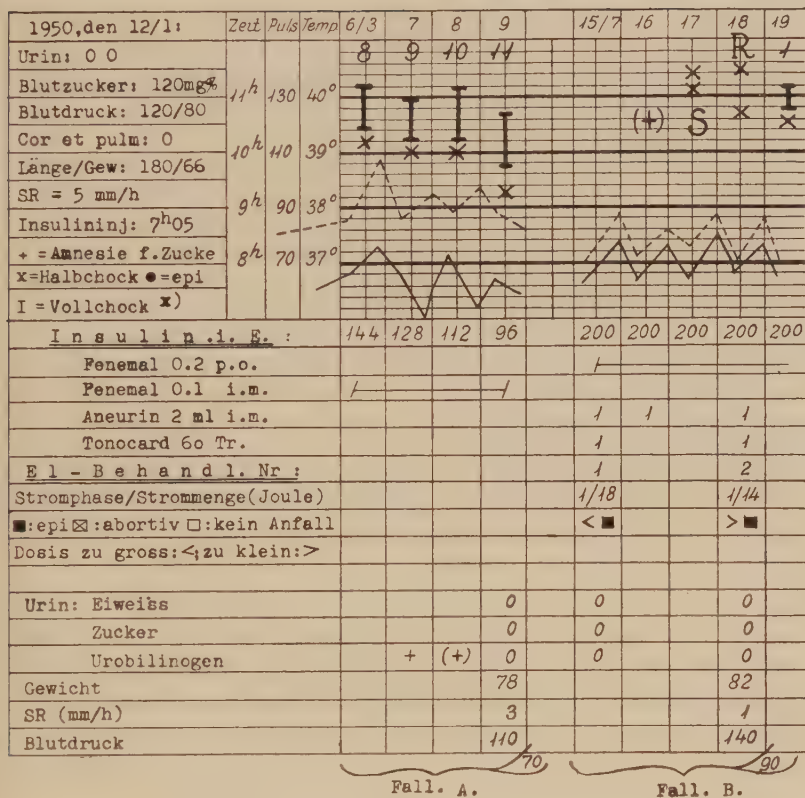
Vorname:

Aufn. Nr: 84/50

geb.

Adresse:

Aufn. Tag: 12/1



*) S = Sensibilisierung (verstärkte Chockwirkung nach Zucker). R = Regulation (Aufwachen ohne Zucker).

Abb. 2.

Beispiel für die Registrierung der Insulinchock- und Elektrochockbehandlung im Puls = Temperaturblatt des Patienten.

Fall A: Sensibilisierung.

Fall B: Kombinationsbehandlung bei insulinresistenten Patienten.

gelten hinsichtlich der „stillen“ Sensibilisierung wie für den Vollchock. Wer daher die „Halbchock“-Zeiten nicht beachtet, begibt sich in die Gefahr, dass sein Patient eines Tages „plötzlich“ lavinenartig sensibilisiert und scheinbar ohne Anlass kollabiert.

3) einfache und übersichtliche *Registrierung* der klinischen Insulinwirkung, s. Abb. 2.

In Fall A ist eine gefährliche Sensibilisierung dargestellt. Man sieht, dass man nach nur 8 Vollchockbehandlungen die Dosis um 32 i.E. senken kann, ohne dass der Chockverlauf beeinflusst wird: der Patient kommt gegen 10 Uhr in Halbchock und gegen 10,15 — 10,20 in Vollchock trotz der stark gesenkten Dosis, also: „stille Sensibilisierung“. Am 11. Vollchocktag tritt zu der stillen Sensibilisierung noch die gewöhnliche Sensibilisierung hinzu, die man daran erkennt, dass die Halb- und Vollchockzeiten *früher* eintreten. Man bekommt an diesem Fall einen guten Eindruck von dem plötzlichen, lawinenartigen Ansteigen der Sensibilisierung: Trotz Senkung der Dosis von 112 bis 96 i.E. eine Verfrühung der Chockzeiten um $\frac{1}{3}$ resp. $\frac{1}{2}$ Stunde, was einer Vertiefung des Chocks bei gesenkter Dosis entspricht. Die Therapie wurde mit 80 i.E. erfolgreich fortgesetzt. Nach 5 Tagen musste die Dosis erneut gesenkt werden, da weitere stille Sensibilisierung eintrat.

Man beachte den hohen Nachmittagspuls und die tiefe, dem normalen Tagesrhythmus *entgegengesetzt* laufende Temperatur. Beides trat kurz vor Beginn der „stillen“ Sensibilisierung ein und verschwand wieder nach Dosissenkung. — Warnzeichen! Ueber Untertemperatur als Mass für die cerebrale Insulinwirkung und insbesondere für die Sensibilisierung vgl. (2).

4) *Maximaldosis* bei insulinrefraktären Patienten: 200 i. e. Infolge der mit unserer Technik schnell eintretenden Sensibilisierung genügt das Abwarten von 1 bis 2 Wochen bei dieser Dosis, um auch die refraktären Patienten mit dieser und auch noch geringerer Dosis in stärkere Hypoglykämie zu bringen. Es gibt verschiedene Mittel, diese Maximal Dosis weiter zu senken. Eines der besten Mittel ist

5) die *Kombination mit Elektrochockbehandlung*.

In Fall B, Abb. 2, ist ein solcher Fall dargestellt. Dieser zeigte auch nach 2 Wochen täglicher Behandlung mit 200 i. E. keine Spur hypoglykämischer Wirkung. Diese setzte jedoch nach einer Elektrochockbehandlung ein, zuerst mit leichter Amnesie, dann mit zunehmender Halbchockwirkung. Nach einer zweiten Elektrochockbehandlung trat auch Insulin-Vollchock ein.

Die Elektrochockbehandlung wurde durch Einführung der Dosierung nach der sog. „Minimaldosis“ zu einem Verfahren ausgebildet, das keinerlei unerwünschte Nebenwirkungen oder Komplikationen hat (5). Die Behandlung wird am schonendsten und klinisch wirkungsvollsten in der Zeit des Insulin-Halb- oder Vollchocks oder in der 4. Insulinbehandlungsstunde gegeben.

6) Zur Sicherheit und Kontrolle wird von jedem Patienten noch

ein besonderes Anzeichnungsblatt geführt, in dem Besonderheiten des Therapieverlaufs vermerkt werden. Insbesondere Zeit und Dauer etwaiger Agitationsperioden und starker klonischer Zuckungen, die möglichst zu beseitigen sind mit Dosisänderung, kleinen Zuckergaben per os oder i. m.¹ und mit Fenemal. Sodann werden die maximalen Pulsschwankungen während der Behandlung, die Weckzeit, besondere Befunde am Herz und Kreislauf sowie die psychischen Befunde notiert. Pulsschwankungen grösser als 25 Schläge pro Min. und eine Weckzeit grösser als 15 Minuten weisen auf Ueberdosierung oder andere Unregelmässigkeiten in dem Behandlungsverlauf hin (Krampf, Agitation) und müssen beseitigt werden. Erythrocyten-Senkung und Blutdruck werden, wenn kein besonderer Anlass vorliegt, zweimal im Monat geprüft, hauptsächlich um Komplikationen fernzuhalten; für den psychischen Krankheitsverlauf haben sie offenbar keine Bedeutung.

7) Beschränkung der Halb- und Vollchockbehandlung. Durch Trainingsbehandlung mit langsam steigenden Dosen, 4 resp. 8 Einheiten jeden zweiten Tag, erhalten die meisten Kranken vor Einsetzen der „Starkbehandlung“ eine 1—2 Monate dauernde „Schwachbehandlung“, die oft schon ausreicht für die Wiedererlangung der körperlichen und psychischen Gesundheit.

Mit diesen Behandlungsregeln ist seit 1 Jahr kein Kollaps und keine Weckschwierigkeit mehr vorgekommen. Nicht eine einzige intravenöse Zuckerinjektion ist nötig gewesen.

Die mitgeteilten Ekg-Befunde betrachten wir als *objektive Begründung* für diese Behandlungsregeln, die dem Wesen nach mit Sakels Phase 1 — „Einschleichphase“ — übereinstimmen und durch v. Braunmühl bereits 1938 eine vorbildliche empirische Darstellung gefunden haben.

ZUSAMMENFASSUNG

1. Es werden elektrokardiographische Veränderungen bei der Insulinbehandlung psychischer Erkrankungen beschrieben, die bei 38 von 69 kreislauf- und herzlabilen Patienten auftraten (die übrigen 31 Kranken zeigten keine EKG-Änderungen).

2. Die Änderungen betreffen hauptsächlich den Vorhof und sind reversibel.

¹ v. Braunmühl gibt (4, S. 25) 5—10 ccm Zucker an. Nach unserer Erfahrung richtet sich die Menge des Zuckers nach der Insulinmenge. Bei kleinen Insulinmengen genügen 2—0,5 ccm Glukose i.m., ja in einigen Fällen sogar 2 ccm physiol. Kochsalzlösung i.m. — Versager bei grossen Insulindosen, woraus sich auch wieder der Vorteil der Behandlung mit so kleinen Insulindosen wie möglich ergibt.

3. Alle Änderungen lassen sich *vermeiden* durch zweckmässige Dosierung des Insulins (Dosisverringierung, sehr langsame Dosissteigerung, „Trainierung“, genaue klinische Beobachtung und Registrierung der Behandlung).

4. Für solche Dosisführung gibt es genügend klinische Zeichen, welche die Anwendung des Ekg überflüssig machen.

5. Diese Behandlungsart hat in 15-jähriger Erfahrung keinen Todesfall ergeben und ist geeignet, auch andere Komplikationen der Behandlung völlig auszuschalten.

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PROBLEMS ASSOCIATED WITH
SENILE DEMENTIA

By

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A lecture given at the annual meeting of the Norwegian Phychiatric
Association in Oslo on august 30th, 1949.

When we survey the shift in age groups which has taken place in the populations of many countries, particularly during the last 50 years, we arrive at a natural explanation of the steadily increasing interest in gerontology, not merely on the basis of social economics and political problems raised as the non-productive part of the population increases at the expense of the younger groups, but also because the increased life-span means a huge increase in the demand for hospital facilities, nursing homes, and homes for the aged. These conditions are fostering a new field of medicine, geriatrics, which is gaining recognition as a specialty.

TABLE 1
Average Life-span.

	Sweden Both sexes	U. S. A. Both sexes	England ♂ ♀		Norway ♂ ♀	
1755/75	34.5					
1789		35.5				
1816/40	41.5					
1850		40				
1871/80					48.3-51.3	
1891/00			44.1-47.8			
1900		50				
1901/10			48.5-52.4			
1911/20	57					
1920		55				
1930		60				
1935	64.3					
1940		64				
1942			61.7-67.4			
1947-					64	-68

A comparison of the numbers of elderly healthy persons with that of the elderly hospitalized shows that persons over 65 years of age in Oslo at the time of the census in 1942 totalled 9.7 %. A count of patients in the same age group occupying beds in hospitals, nursing homes and homes for the aged in Greater Oslo as of Feb. 19, 1947, totalled 29.2 % (Table 2).

TABLE 2

Age	Oslo's Population as of Dec. 1, 1942			Hospital Census as of Feb. 19, 1947		
	♂	♀	Total	♂	♀	Total
0-14	14.1	10.9	12.3	6.5	3.5	4.7
15-29	25.1	23.9	24.5	13.6	14.5	14.1
30-44	28.3	28.5	28.4	23.1	24.2	23.8
45-64	24.4	25.7	25.1	32.0	25.6	28.2
Over 65	8.1	11.0	9.7	24.8	32.2	29.2
Total	100	100	100	100	100	100

Although the first table includes Greater Oslo and the second Oslo alone, and although there is a time difference of 4 years, the table nevertheless may be assumed to give a good picture of the excess of the older age-groups hospitalized.

The increased life-span and reduced birth rate will, according to statistics worked out by the Central Bureau of Statistics, presumably result in an increase in total population of about 300,000 from 1945-75. Approximately 200,000 of these individuals will be over 65 years of age (Table 3).

TABLE 3

	0-14	15-64	Over 65	Total
1945	676,000	2,100,000	282,000	3,058,000
1975	625,000	2,257,000	478,000	3,360,000
	÷ 51,000	+ 157,000	+ 196,000	+ 302,000

While a total of all age-groups will presumably increase by 9 %, the numbers of persons over 65 years of age will have a presumed increase of 66 % in the period from 1945-75, that is from 9 % to 14 % of the population. When these figures are compared with the presumptive figures for U.S.A. and England, we find a marked similarity in the estimates (Table 4).

TABLE 4

Norway	1945-75	9 %-14 %	
U.S.A.	1940-80	6.8%-14.4%	(Cowdrey)
England	1951-71	11.6%-17 %	(Lewis)

A hospital count as of Feb. 19, 1947, in Greater Oslo showed that patients over 65 years of age constituted 29.2 % of the total. Using the statistical figures for the increase in the population over the age of 65, a rough estimate leads us to expect that the patients over 65 years of age will require about 45 % of all beds in 1975.

As the life-span of the population increases we see more and more of the psychic defect conditions accompanying old age. In order to study more closely the problems of senile dementia, especially the prognosis for these patients, we have at Dikemark Hospital, Women's Department, determined the number of patients over 60 years of age admitted to the department during the last 20 years (1929-48), the length of time spent in the department by those with a diagnosis of senile dementia, and studied in detail the case histories of 100 women patients admitted for the first time to the department (1942-48) with a diagnosis of senile dementia. Some general remarks follow:

The number of first admissions over the age of 60 in our asylums (all diagnoses), in percentage of all patients admitted, has increased from 11.0 % to 16.7 % in the 3 five-year periods from 1931-45. During the same period the percentage of first admissions with diagnoses of involutional and senile psychoses rose from 7.5 to 10.6 % of all first admissions (Table 5).

TABLE 5

Number of first admissions in our asylums in % of all first admissions.

	Over 60 — All Diagnoses			Involutional and Senile Psychoses		
	♂	♀	Total	♂	♀	Total
1931-35	10.0	12.1	11.0	5.8	9.2	7.5
1936-40	10.4	14.2	12.3	6.8	10.8	8.8
1941-45	15.9	17.6	16.7	9.4	11.6	10.6

There is thus an increase in psychoses of the aged in this period of over 40 % for both sexes, which is significant enough, though it is not as alarming as the figures from New York's Civil State Hospitals

where, according to *Bechenstein-Gold*, the percentage of first admissions with the diagnoses senile psychosis and arteriosclerotic dementia increased from 13.5 % in 1913 to 37.9 % in 1943, i.e. an increase of 280 %, or the figures from Oringe Mental Hospital in Denmark which, according to *Östergaard Jensen*, showed an increase in admissions of psychoses of the aged in the 4 five-year periods 1927-46 from 3.59 to 10.13 % or an increase of 182 %.

The physiological background for the changes of old age is found in the organism of the elderly in marked chemical and pathologico-anatomic changes which form the basis of the psychic defect conditions. It is often difficult to determine from the symptoms where the normal psychic changes of age end and the changes of disease begin. The diagnosis senile dementia includes 2 roughly separate disease entities, the simple dementia or parenchymatous form and cerebral arteriosclerosis with demential changes. The distinction between the two forms was first outlined by *August Hoch* in 1912. Often, perhaps most frequently, these two forms are combined, so that the disease is termed a predominantly parenchymatous or predominantly arteriosclerotic dementia rather than being a distinct differential diagnosis used but the differentialization is important from a practical point of view. The criteria we have drawn up to distinguish between the two diagnoses are as follows: *Simple dementia* usually begins after the age of 65. It has an insidious beginning. There is reduced power of attention and learning (presbyophrenia), reduced memory, especially for recent events, later amnesia or return to childhood. Further symptoms are confabulation, logorrhea, reduced will power, poor judgment, emotional lability, apraxia, psychotic complications consisting of confusion, paranoid behaviour and generally increasing dementia. *Arteriosclerotic dementia* begins most commonly at about or after the age of 60. It is characterized by either (1) an acute beginning associated with an apoplectic attack, or more insidiously with (2) a preceding neurasthenic phase with increased fatiguability and irritability, headache, dizziness, anxiety, and sleep disturbances. Sufficient rest causes recession of symptoms but psychotic complications with confusion and paranoid signs may arise. Later there is reduced mental capability, especially reduction of the power of concentration, but in contrast to those suffering from simple dementia, the personality and insight into the disease are better preserved. There may be focal symptoms. Hypertension is most commonly found. Progression includes loss of memory, emotional incontinence, depres-

sive syndromes and temperamental indifference. Later there is increasing dementia, often in waves with remissions and exacerbations.

At Dikemark Hospital there has been a marked increase in the numbers of women over 60 years of age admitted during the last 20 years, an increase from 15.8 to 23.9 % of the total admissions (Table 6).

TABLE 6

	Total admissions ♀ over 60 years of age		Senile dementia of the preceding		Total admissions	
	Pts.	%	Pts.	%	Pts.	%
1929-33	100	15.8	66	10.4	634	100
1934-38	176	17.8	111	11.2	987	100
1939-43	228	24.5	120	12.9	929	100
1944-48	183	23.9	98	12.8	767	100
(Oringe, Denmark	1942-46)	(18.3)		(10.1)		(100)
at Dikemark						
on Aug. 4, 49	115	24.8	40	8.6	465	100

There were not many patients under the age of 60 with a diagnosis of senile or presenile dementia. In the entire 20-year period 1929-48 with a total of 445 women admitted as suffering from senile dementia there were only 50 patients under 60 years of age, namely 44 (9.9 %) with arteriosclerotic dementia and 6 (1.3 %) with presenile dementia. Apart from this I shall not consider presenile dementia here, but merely mention that *David Henderson* believes that the Alzheimer-Pick group has increased markedly in recent years.

A study of the duration of hospitalization for patients suffering from senile dementia in the 10-year period 1929-38 shows that more than half of the patients were discharged within 6 months, three fourths within 1 year (Table 7).

TABLE 7

Duration of hospitalization		No. of Pts.	%
Under ½ year		100	56.5
½-1 "		31	17.6
1-1½ "		6	3.4
1½-2 "		10	5.6
2-3 "		13	7.3
3-4 "		8	4.5
4-5 "		3	1.7
Over 5 "		6	3.4
		177	100

As an illustration of the acute lack of nursing home beds it should be mentioned that on Aug. 4, 1949, 80 (70 %) of the 115 patients over 60 years of age in the department could have been discharged to a nursing home and that the duration of hospitalization of the senile demented over 60 years of age from 1929-38 averaged 1.30 years per patient, while the average duration of the 40 patients in the department on Aug. 4, 1949, is so far 2.95 years per patient.

It is of interest to examine the immediate grounds for hospitalization of the senile demented in order to find a basis for a future prophylaxis if possible. I shall therefore attempt to review the situation leading to admission, the clinical picture, and the situation at the time of discharge of 100 women, first admissions over 60 years of age, with a diagnosis of senile dementia. In the following tables the letter A is used to denote arteriosclerotic dementia, and the letter B to denote simple dementia. The first table shows the distribution according to age and diagnosis (Table 8).

TABLE 8

Age	A		B		Total
	Pts.	%	Pts.	%	
60 -69	28	38	6	23	34
70 -79	31	42	14	54	45
Over 80	15	20	6	23	21
	74	100	26	100	100

TABLE 9

Duration of Illness before Admission

	A		B		Total	
	Pts.	%	Pts.	%	Pts.	%
Under 1 mo.	10	14.7	0		10	10.6
1-6 "	13	19.1	0		13	13.8
½-1 yr.	9	13.2	4	15.4	13	13.8
2 "	12	17.7	8	30.8	20	21.3
3 "	8	11.8	4	15.4	12	12.8
4 "	6	8.8	5	19.2	11	11.7
5 "	2	2.9	2	7.7	4	4.3
Over 5 "	8	11.8	3	11.5	11	11.7
Total	68	100	26	100	94	100
Unknown	6				6	
	74		26		100	

As anticipated we found that arteriosclerotic dementia begins earlier than simple dementia and that three fourths of the patients have predominantly arteriosclerotic and one fourth predominantly simple dementia.

The figures in Table 9 show that 34 % of the patients with arteriosclerotic dementia were admitted after less than 6 months duration of illness, 15 % within, the first month of the onset, while the duration of the disease in all cases of simple dementia was over 6 months previous to admission.

TABLE 10
Patients' Housing at the Time of Admission.

	Alone	With Family	Nursing Home	Family ward	Unknown	Total
A	18	33	16	3	4	74
B	—	16	7	2	1	26
	18	49	23	5	5	100

It is interesting to note from Table 10 that almost 25 % of the patients with arteriosclerotic dementia lived alone at the time of admission, indicating that the acute and often alarming symptoms necessitate rapid hospitalization and do not give time or opportunity for family or nursing home care.

TABLE 11
Provoking Social and Psychic Factors.

	A	B	Total
Economic difficulties	10	1	11
Death of near relative	5	2	7
Gov't. enforced billeting	3	1	4
Marriage of children	4	—	4
Outbreak of war, 1940	3	1	4
Filipstad explosion, 1943	2	1	3
Feeling of loneliness	1	1	2
Mental illness of sister	2	—	2
Peace, 1945 (Nazi sympathy)	1	—	1
Shock due to loss of dental plates	1	—	1
	32	7	39
% of the number of patients	43%	27%	39%

We find here also, as might be expected, a preponderance of the patients with arteriosclerotic dementia. The actual proportionate importance of the factors listed cannot lead to specific conclusions since,

for instance, the feeling of loneliness is without doubt a more influential psychic factor than is indicated in our case histories.

TABLE 12
Provoking Somatic Factors (Situation Leading to Admission).

Fall caused by dizziness	5
Symptoms of cerebral hemorrhage	3
Malnutrition	3
Fever	1
Pneumonia	1
Fracture	1
Operation for hernia	1
Cerebral concussion after motor accident	1
Total	16

All of the provoking somatic factors occurred in patients with arteriosclerotic dementia, while no such factors were recorded as having bearing upon the admission of patients with simple dementia.

The information concerning the endogenous factors was insufficient to show any familial tendency towards cardiovascular diseases in the case of arteriosclerotic dementia, but a hereditary tendency to mental illness in the immediate family (parents, siblings, children, grandparents, sibling of parents) was clear in the patients with senile dementia, as it was found in 24 % (Table 13).

TABLE 13

	Total No. Pts.	No Information	Remainder	Mental Illness in family	%
A	74	9	65	15	23
B	26	5	21	6	29
	100	14	86	21	24

7 of the 100 patients with arteriosclerotic dementia had a history of a previous psychotic period, 6 depression and 1 postpartum psychosis.

As shown in Table 14 restlessness is the chief reason for admission, i.e. a total of 67 %. It appears that most of the remaining 33 % could have been cared for in suitable nursing homes.

Of the clinical findings noted in these patients while in the department we shall only consider blood pressure and blood sedimentation

TABLE 14
Chief Cause of Admission.

	A	B	Total
Restlessness	51	16	67
Uncleanliness	5	4	9
Paranoid ideas	6	—	6
Danger of suicide	4	2	6
Refusal of food	4	—	4
Lack of nursing home space	—	3	3
Danger of fire	3	—	3
Economic reasons	1	1	2
	74	26	100

rate. The blood pressures recorded on the second day are used here to give a basis of comparison. The blood pressures were taken in the morning with the patients fasting and lying in bed (Table 15).

TABLE 15

RR	Systolic		Diastolic		Total
	A %	B %	A %	B %	
Under 150	23	23			23
150-174	36.5	46			39
175-199	13.5	27			17
200 and over	27	4			21
	100	100			100
Under 90			21.6	30.8	24
90-99			24.3	30.8	26
100-109			25.7	19.2	24
110 and over			28.4	19.2	26
			100	100	100

Approximately three fourths of the total number of patients had a systolic blood pressure of over 150 and a diastolic pressure of over 90. As might be expected there was an excess of especially high blood pressure values among the arteriosclerotics.

The blood sedimentation rates taken during the first week after admission show noticeably high values. 73 % had sedimentation rates of over 10 mm., and 46 % had sedimentation rates of over 20 mm (Table 16).

TABLE 16

SR	A %	B %	Total %
0-10	27	24	27
11-20	27	24	27
21-30	18	12	16
31-40	16	20	17
41-50	2	4	2
Over 50	10	16	11
	100	100	100

For purposes of comparison it may be mentioned that *Jörgen Ravn* in his material from Nyköping found sedimentation rates over 10 mm. in approximately 54 % of his patients with arteriosclerotic psychosis, but in his study patients with demonstrable somatic complications were excluded. Some investigators (*Eckerström*, *Westergren*) maintain that especially high sedimentation rates are not found in the aged, while on the other hand others (*Dahlberg*, *Hölzer*) claim that there is normally a physiological increase with age. Even though the latter claim may be correct, it does not explain the high sedimentation rates found in this study, but since this material has not been investigated with that particular problem in mind, we cannot evaluate the significance of the high sedimentation rates.

A survey of the types of psychoses seen in the department after the acute phase was passed showed that 45 % of the patients were marked by their dementia alone, while the remainder showed a more distinct development of the symptoms (Table 17).

TABLE 17

	A	B	Total
Dementia alone	30	15	45
Euphoria	13	5	18
Depression	15	2	17
Lability	10	3	13
Paranoia	6	1	7
Total number of patients	74	26	100

Finally we shall consider the duration of treatment (Table 18-19). It is of especial interest that 32 of the 74 or 43 % of the patients with arteriosclerotic dementia were discharged within 3 months, 41 of the 74 or 55 % within 6 months and 51 of the 74 or almost 70 % were discharged within 1 year.

TABLE 18

*Duration of Treatment and Disposition after Discharge of 100 Women
First Admissions over 60 Years of Age (1942-48).*

A	Deceased	Home	Family ward	Homes for Aged Nursing Homes	Total discharged	In Dept.
Under 1 mo.	3	4 (2)	1	2 (1)	10 (3)	
1-2 "	1	4 (2)	2	2	9 (2)	
2-3 "	—	6 (2)	6 (4)	1 (1)	13 (7)	
3-4 "	2	2	1	—	5	
4-5 "	—	1	1	—	2	
5-6 "	1	—	1	—	2	
½-1 yr.	1	3	3	3	10	1
1-2 "	5	—	2 (1)	—	7 (1)	3
2-3 "	2	—	—	—	2	3
3-4 "	—	—	1	1	2	1
4-5 "	1	—	—	—	1	2
5-7 "	—	—	—	—	—	1
No pts.	16	20 (6)	18 (5)	9 (2)	63 (13)	11
%	25	32	29	14	100	

The figures in parentheses denote patients readmitted to the department. For the predominantly parenchymatous form there are too few figures to make a comparison possible, but the majority of these patients remain in the department from 1-3 years (Table 19). 68 % of them die in the department after the first admission as against 25 % of those with predominantly vascular disease.

TABLE 19

B	Deceased	Home	Family ward	Homes for Aged Nursing Homes	Total discharged	In Dept.
Under 1 mo.	1	—	—	—	1	
1-2 "	—	—	—	—	—	
2-3 "	—	—	—	1	1	
3-4 "	1	1	—	—	2	1
4-5 "	1	—	—	—	1	
5-6 "	1	1 (1)	1	—	3 (1)	
½-1 yr.	4	—	—	—	4	2
1-2 "	1	—	1 (1)	1	3 (1)	1
2-3 "	4	—	—	—	4	
3-4 "	—	—	—	—	—	1
4-5 "	—	—	—	—	—	
5-6 "	—	—	—	—	—	2
No. pts.	13	2 (1)	2 (1)	2	19 (2)	7
%	68				100	

Those readmitted, which in the case of A were 20 %, had been out of the department an average of 10 months before readmittance. Both the table for duration of disease before admission and duration of treatment for first admissions show similarity in numbers with statistics from all Norwegian mental hospitals.

The causes of the 29 deaths were distributed as seen in Table 20 with pneumonia as the leading cause of death.

TABLE 20

	Pneumonia	Marasmus	Acute enteritis	Thrombosis Apoplexy	Following fracture	Myocarditis	Subphren. abscess	Total
A	7	2	2	3	—	1	1	16
B	5	4	2	—	2	—	—	13
	12	6	4	3	2	1	1	29

There has so far been no causal therapy for senile dementia apart from rest, care, and general medical treatment of concomitant organic complications. Burlingame claims that he has had good results in 12 % with the use of large doses of 15 % NaJ i.v., but we have not yet been able to try this treatment at Dikemark.

What conclusions can be drawn from this study?

In the first place we find that there are several exogenous factors in the admission situation which might be amenable to prophylactic treatment.

Furthermore, and with special reference to the prognosis, we find that the duration of treatment in the department is short for arteriosclerotic dementia, which makes up three fourths of all first admissions of women with senile dementia. In addition to these there are a number of women with senile dementia who do not reach Dikemark but are discharged after short hospitalization directly from Ullevål's psychiatric department (Oslo Municipal Hospital) to their homes or to suitable nursing homes, a circumstance which makes the prognosis even more favourable than is apparent from the results in this study.

In regard to the exogenous factors: There has been a tendency to accept old age as the primary cause of the psychic diseases which trouble the aged, while the exciting cause at least, apart from other organic diseases and malnutrition, should often be sought in what is known as "lack of social integration", namely the psychic stress which accompanies loneliness, unemployment, the feeling of uselessness, of being a burden to others, lack of association with their equals on their own level and with the constant comparison of themselves with people of a younger generation. *Vischer* cites *Burdach* who wrote in 1825: "But as the years go by a great proportion of the old man's contemporaries die, and he finds himself alone, in the midst of a generation formed under different circumstances, whose ideas and manners are alien to him, and with which he has few points of contact, if only by reason of the difference of age". These are points of view with which we agree after making our investigations. *Lawton* says, "Our life is not a book with old age the last chapter, rather a series of books, a sequence of short stories, each with its own adventures, its own consummations." The purpose of geriatrics is thus not only to help the ailing aged but also by prophylaxis to prevent illness in the aged. In order to do this it is important to give old people conditions that reduce the lack of social harmony to a minimum. There appears to be an increased tendency for the aged not to be supported by their own kin, and it becomes important for society in its efforts to help the aged to seek to compensate for the loss which occurs when the old person is no longer a part of the family unit. The English have attempted to do this by organizing large clubs where old people who are lonely or need a change of environment may gather daily with others in similar circumstances, and where they may have their meals, find a little work and entertainment and have a place to resort to without danger to their independence or personal freedom.

With regard to the psychotic phase we found that one third of the senile demented were admitted for reasons mainly arising from the lack of other suitable nursing home space. In addition to these, although two thirds were admitted for restlessness, these manifestations are very often of such a nature (knocking on the walls, abuse of neighbours, etc.) that the patient might well be treated in a suitable nursing home or department instead of a mental hospital. This is especially true of the arteriosclerotics whose psychotic symptoms are often passing phenomena and short-lived. *Per Hanssen* has pointed out the desirability of establishing a nursing home department for the aged in close connection with a geriatric department in the medical centres.

If there were a possibility of isolation in these nursing home de-

partments, as also suggested by American and English authorities, some of the psychic complications of cerebral arteriosclerosis could be dealt with in such departments. Apart from easing the burden on the more valuable mental hospital beds, the patient and his family would also thus be spared the trauma accompanying confinement to a mental hospital. A special committee appointed by the British Medical Association to investigate the problems of the aged says in its report of 1947, "The Committee considers it unreasonable that cause should be given for such distress (confinement to mental hospital) when the member in question is merely a victim of mental deterioration associated with old age."

In conclusion the desirability of the following is expressed:

1. Prophylactic measures to prevent lack of social integration.
2. Increased number of homes for the aged and nursing homes.
3. Isolation rooms for the temporary psychoses of the aged in nursing homes connected with medical centres.

S U M M A R Y

After briefly surveying the increased life span, the higher ratio of elderly persons to the young and the consequences upon the population of the Norwegian mental hospitals, the author reports his investigations of 100 female patients (first admissions 1942-48) over 60 years of age treated at Dikemark Mental Hospital under the diagnoses of arteriosclerotic and simple dementia. The importance of exogenous factors leading to admission is stressed as well as the fact that one third of the patients were admitted for reasons which might have been dealt with in suitable homes for the aged. Many of the remaining two thirds, whose main reason for admission was restlessness, might also have been spared confinement to a mental hospital if isolation wards for short-term treatment had been available in nursing homes attached to medical centres, especially in that 43 % of the patients with arteriosclerotic dementia were discharged within 3 months, 55 % within 6 months and nearly 70 % within 12 months after admission.

The author concludes by emphasizing the desirability of better prophylaxis, more homes and wards for elderly patients with isolation rooms for temporary psychoses.

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REMARKABLE PATIENTS TO WHOM HYPNOSIS BROUGHT RELIEF

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"The longer one practises the more one experiences that the psychical condition of the patient has a very strong and sometimes predominating influence on nearly all diseases."

This sentence, which would be taken straight from the heart of a psychiatrist and which is not mine, but is in accordance with a judgment passed by me (1), comes from the internist Schalijs (2). He, however, adds: "especially this is the case with the gastric ulcer."

This addition is to me a proof that Schalijs was not in a position sufficiently to observe this influence in the same way with gastric ulcer as with other physical diseases, otherwise he had left it out. The internist Groen (3) has pointed out the powerful influence of the psyche in the case of colitis ulcerosa. But indeed it can be said of every organ and of every disease, that the influence of the soul on it is powerful, even if that influence is not clearly perceptible in everybody. In this respect I should not give a definite preference to the stomach.

Below I shall mention some remarkable syndromes in which that influence of the soul on the body, as proved by the beneficial influence of hypnotical treatment, was very striking.

The 48-year-old Mr. A., an accountant, came to me on 28.12.'45 at the desire of his wife. He himself thought a neurologist nonsense, because "his nerves had never yet troubled him." From the end of July he had not been a single day without a violent pain in the gastric region. He often vomited. For many years he had already been treated for this pain, which often stayed away for months, by various gastro-enteric specialists. The Röntgen-photos had shown a small niche at the duodenum. The pain always started about 2 hours after eating. He used enormous quantities of bicarbonate of sodium and aspirin to remove the pain, without much success. When the stomach-ache was gone, he sometimes got violent neuralgia in the second and third trigeminus-branch on the right. None of the treatments had had any noticeable effect. Formerly he sometimes worked 36 hours at a stretch,

of late years 12-14 hours a day, also on Sundays, always to the minute. He ate in a great hurry, always rose from table before the others had finished, never took any recreation. I prescribed him a normal mode of living with some pleasant recreation, eating quietly and never hastening.

After 2 hypnoses he has no more vomited, has had no more pain in the region of the duodenum, except when he received an assessment of the inspector of taxes for a security he could not pay. I expressly state the cause of this emotion, because some practitioners, a.o. Groen, are of opinion that a definite kind of emotion causes symptoms in a definite organ, another sort of emotion again in another organ. My experience is different, viz. that all emotions in the same patient always give cause for complaints in the same organ, so that the, for that matter, meaningless conception "inferior organ" has some sense after all. After that the patient has never been troubled any more, not even by his trigeminus-neuralgia, which I also drew into the hypnotical suggestions afterwards.

Having been one year without complaints, I discharged him as recovered at the end of December. With this patient it was further remarkable that by suggestion in hypnosis and by drinking a glass of cold water every morning after getting up, he recovered from the obstipation from which he had suffered for many years. According to my suggestion he got a motion every day promptly at 8.30. Also this recovery has maintained. (4).

Miss B., seamstress, 32 years old, came to be treated by me on 10.5.'46, because she had a stomach-ache after every meal and threw up everything again, even a cup of tea. Her complaints had started more than 6 years ago. The internist wrote to me: "In August '39 Miss B. came to me for the first time on account of stomach-complaints. Röntgenologically: a distinct 6-hour rest and a slightly deformed praepyloric part. As the stool always contained occult blood till March 1940, the pain increased and the weight decreased, a proof-laparotomy was decided upon, with which no defect of the stomach was found(!). In connection with anamnesis and investigation resection was nevertheless decided upon. Neither were defects found in this preparation. When she was dismissed, the patient was without complaints, but in September '40 she fell ill again. She often vomited. This vomit had a high acidity-content, the urine showed a strong urobilinogen-reaction, the stool did not contain occult blood now, and the blood was, as always, normal. Röntgen-photo: a somewhat slow-working gastro-enterostomy with a retrograde motion of pap in the duodenum. The patient was informed: "deformations". She was treated till March 1943 without success. After that the patient vomited blood in 1943, which was repeated in September 1944. She was operated upon once more. The old gastro-enterostomy was substituted by another, but directly after the operation the vomiting started anew, for which reason she lost much weight. Therefore she was operated upon again for the third time 3 months later, the deformations being removed. A week afterwards the vomiting was as violent again. A few months afterwards she was operated upon anew in order to open an abscess caused by the operation. Her condition had not improved. In April followed the 7th operation, when a second gastro-enterostomy was done. After a fortnight a large abscess low in the belly had to be opened rectally. When this appeared to have been insufficiently opened, it was therefore opened anew (9th operation) after blood-transfusion, because the patient's condition was so poor. Shortly afterwards an abscess at the abdominal wall had to be opened (10th operation). Having been in hospital for 7 months, she came home on 15.8.'45. At first everything was all right for 4 weeks, then the vomiting started again.

When she came to me on 10.5.46 she weighed with her clothes on 43 kg (height 1.65 m). She had distinct symptoms of pellagrosis; very distinct brown discolorations on the legs and the face, some more reddish at the back of the hands, chaps in the lips. She had 4.5 million erythrocytes, a haemoglobin-content of 63, index 0.63. There were slight, but distinct deep joint sense disorders in the big toes. From her family-doctor she already twice a week got an injection of Pernaemon forte 2 cc. and 3 times daily 50 mgr. vitamin B₂. As the journey by train was very fatiguing for her, she was treated only 3 times a week. The treatment consisted on eating 6 slices of bread with some meat and an egg in hypnosis, during which the necessary suggestions were given and after which she remained lying in hypnosis for 2 hours. While she was with me she only vomited in hypnosis a few times. After some weeks the vomiting at home also decreased, the pain abated, and the pellagrosis was cured. In a much improved condition, she broke off the treatment with me in the beginning of November because she took up her work again and went to live elsewhere.

How the case under discussion should originally have been diagnosed, is not quite certain after all. It is certain, however, that she was hysterical and should never have been operated upon. Hysterical patients often have a craving for operation, this was also distinctly the case with this patient. She told me once that she vomited at home and asked me if she was to be operated upon again. According to her aunt, with whom she lived, she had tampered with menstruation-blood in the W.C. in order to give her an impression of blood-vomiting. When I did not pay any attention to her information about blood-vomiting, it did not occur again and she no more spoke about it.

One day I was consulted by a patient with abdominal complaints who asked me for a certificate that I thought it necessary that he was operated upon. He had been submitted to 12 abdominal operations and the surgeon who had been consulted, first wanted to have a certificate by a psychiatrist before operating upon him for the 13th time. The patient refused any treatment; he only wanted to have the certificate!

A hysterical patient of Schultz was even 24 times subjected to laparotomy.

The 44-year-old Mrs. C., whom I had treated for all kinds of nervous complaints for some years, in 1941, when I was not allowed—on account of German regulations—to treat her further, got rheumatism of the left pulse-joint. In spite of intensive treatment by a homoeopathist, a surgeon, and a specialist for rheumatism for more than a year, the condition of the joint, when she came to be treated again by me in 1945, was bad. The pulse was monstrously swollen; the muscles of the left forearm, as well as of the upper arm, were distinctly atrophic: the fore-arm was 2½ cm, the upper arm 1½ cm thinner than the right arm and there was also distinct atrophy of the thenar muscles on the left. The mobility of the pulse-joint was greatly limited, the pain was so violent that she could not do anything with the hand, could not even take up something. From the 2nd hypnosis onwards the pain left her and after a few weeks she could use the hand for everything again without pain. The atrophy disappeared within a few months. A few months later the right pulse-joint began to swell painfully, just as the left

pulse-joint used to do. With a few hypnotical treatments pain and swelling disappeared. Until now, after about 5 years, her recovery has lasted.

This case of recovery from rheumatism by hypnosis is not unique, as appears from the following case:

Miss D., 63 years old, came to me on Oct. 31st '46 on account of rheumatism in her left knee-joint, from which she had suffered since December 1945. Moreover she had a congenital hip-luxation left. Radiation for some months by a physico-therapist had not given any improvement. When she came to me, she walked with a stick and was greatly crippled on account of pain in her knee. The right knee was 6 cm thicker than the left. As the sediment was normal. I decided not to give gold. She was hypnotized twice a week and radiated about 20 minutes with infrared rays. From the 2nd treatment onwards the pain lessened. After the 3rd treatment the pain subsided distinctly and after a 7-week treatment pain and swelling had completely disappeared.

I attribute this quick recovery to the hypnosis and not to the few radiations, as before that, she had been radiated for many months without success. Also van Breemen calls attention to the great influence of the psyche in his book (5): "Mrs. D. 45 years old. Her husband, who seems to be in good health, suddenly falls dead in her arms. After some weeks a chronic arthritis of all arm-joints develops with typical rheumatological characteristics. All other joints remain quite normal".

The following remarkable case of eczema could be cured by hypnosis.

Mr. E., works manager in a firm for hydraulics, came on 16.1.'46, 50 years old, to be treated by me on account of eczema that covered his whole body, also between the hairs of head and beard. He had always been in good health, till a year before, in February 1945, he experienced a great shock. During a German razzia he had hidden a few young men. When the soldiers found them in his house, he was to be shot on the very spot. The guns were aimed at him already, but he gave the soldiers a bottle of gin, and having made them drunk, he was left by them. The day after this shock he had eczema on his whole body on account of which he had to give up his work. He could sleep no more from itching and the attacks of sweating that tormented him night and day, he became cryish and irritable and could not bear to have his clothes on. Every few weeks he got new eruptions at different places of his body, sometimes also thickenings of the skin, which were attended by redness and high fever and with which also local glandular swellings were seen. In spite of treatment for almost a year by two dermatologists, there was no improvement. Having been nursed in a clinic in December 1945 the elephantiasis disappeared but otherwise everything remained the same.

When he came to me by motorcar, in pyjamas, and wrapped in a blanket, he made the impression of a human wreck. He was treated for some weeks five times, after that for some weeks 3 times a week and finally twice a week. The treatment consisted of "passes" during the, with him, deep hypnosis with which I first touched the front of his body, after that, when he lay face downwards, the back, always 10 times after which I left him lying in hypnosis for 15-30 minutes. No further treatment was given except some talcum and, in the beginning, an unguent on the open spots prescribed by the family-doctor.

From the first hypnosis onwards recovery set in. A few times he still had a slight recidivation with redness and fever. He could sleep again, the itching and the attacks of sweating stopped. After 6 weeks he could again work for half days and after three months whole days again. The treatment was stopped in November; recovery has maintained.

In case of congenital organic disorders of the central nervous system, much success usually cannot be expected from hypnotical treatment. That an attempt in this direction can be, nevertheless successful, appears from the following case.

A girl F., 17 years old, office-clerk, came to me for treatment on 13.4.'46 on account of writer's cramps; as soon as she began to write, her right arm as far as the shoulder became tired to death. As early as from her 4th year she had great tic-movements in her face as soon as she began to speak, especially to strangers, her speech thus being very difficult and indistinct. She is stiff and awkward with everything, could never join at gymnastics at school. She can learn very well, never had to double a class, has finished a 4-year advanced elementary school. She can play the organ but not the piano, because this goes too fast for her. Only of late she has been able to fasten her boot-laces. She has never had a brain-disease.

When I examined her I found her very slow in all her movements. There appeared to be dysdiadochokinesis. The attitude of her hands was typical, as in case of "athetose double". The fingers could not be kept still. When walking she did not move her arms as usual.

The serious disorder in her writing appears from fig. 1.

Kromme Waal
Amsterdam

My diagnosis was: congenital striatal affection.

The treatment consisted of hypnosis twice a week and practising before the mirror at home in order to keep the face-muscles silent. After a few weeks the tics had almost disappeared and the writing had very much improved, as shown in fig. 2. Writing was no longer fatiguing for her.

Kromme Waal
Amsterdam.

Also in case of common writer's cramp, which is considered to be a "functional" affection, hypnosis often causes improvement in rather a short time. The question is whether these cases are indeed only

functional, or whether—under this syndrome—there are very slight organic aberrations of the corpus striatum, perhaps on a predestined basis. The torticollis “cerebralis”, which a short time ago was considered functional, is as a matter of fact now also thought of as an organic affection.

Mr. G., 62 years old, retired teacher of calligraphy and correspondent, came to be treated by me on 9.9.'46 on account of writer's cramp from which he had been suffering increasingly for 3 to 4 years. He was treated by 2 nerve-specialists: one of them said that he should only write in capital letters and regularly electrified him; the other said that he ought not to write at all for eighteen months, which advice he followed. His writing did not improve, however. When he came to me, his writing was, for an ex-calligraphist, bad (fig. 3); he could only write extra-

Jacob Marinestreet
Amsterdam

ordinarily slowly and trembled when doing it. Moreover he drew his face to the left and his right shoulder up when writing: so he got a torticollis. I advised him never to be in a hurry any more. The treatment consisted in hypnosis 3 times a week, after a fortnight twice a week. After 6 weeks his writing was normal again, though he wrote somewhat more slowly than before (fig. 4). The torticollis when writing has almost disappeared.

*werk. Door schade en schande wordt
men wijs. Als het hek van den dam is,
loopen de varkens in het koren.*

The girl H. came to me on 24.9.'46, 14 years old, on account of heavy vomiting, which had begun when she was eighteen months old. From her 7th till her 9th year the vomiting had almost stayed away but the last 5 years the vomiting had grown much worse again. She had been in hospital for this vomiting in 5 different clinics a.o. in a University Children's Clinic, without any improvement. Disorders were not found anywhere. Usually the vomiting began after she had not vomited for a week. In the first year she was at most sometimes a fortnight without vomiting. During such a period of vomiting she continually vomited for 4-5 days also in the nights. She then threw up a coffee-coloured vomit. She could not retain anything, not even water. During those days she had no urination and no stool. After 3-4 days her condition was very bad she seemed to be dying. Then the vomiting suddenly stopped and she could eat and drink everything again. In a few days she had again recovered her loss of weight. The family-doctor wrote to me: “Perhaps it is a neurosis of the stomach.”

When I carefully took up the anamnesis, the very intelligent girl told me that

the periods of vomiting always began with a preceding bad headache and a shyness of light. This made me diagnose migraine. I treated her in hypnosis with suggestions relating to migraine, and asked the family-doctor, if the attacks should come back, to inject Gynergen. As she lived out of town, she could at most come twice a week and that not even always. Therefore I gave her a bottle of "magnetized" water to take with her, which her mother was to rub on her head and in the abdominal region twice a day, when she lay in auto-hypnosis. The attacks became less frequent and less violent. From the family-doctor she got in the beginning 9 injections of Gynergen of 0.25 mg, 2 injections for each attack. Since then, now 8 months, she has remained free from each complaint¹.

This is indeed a remarkable case of migraine, so remarkable that also in the clinics the doctors diagnosed neurosis of the stomach. In this place I call the attention to the fact that also with common forms of migraine I have very often been able to attain recovery by hypnosis. Many patients have been obliged, however, to break off their study or career and very much regretted not to have heard about hypnosis years ago.

Mr. I., an accountant, 58 years of age, came to me in the autumn of 1941, because when walking he had such heavy attacks of pain in his chest, radiating to his back, that he had to stand still every few minutes. He could not even wear an overcoat because the pain became worse when he had it on. I directed him to a heart-specialist, who diagnosed angina-pectoris vera and treated him for that with medicines. As there was no improvement, the patient came back to me again in June 1942, after having given up the treatment by the heart-specialist. I treated him exclusively with hypnosis twice a week, after 3 months once a week, till April 1943. The pain lessened already after the first hypnosis and stayed away completely after 4 months. He could again take long walks without pain, also when wearing a heavy overcoat. The pain has never returned. In 1945 he passed the test for the East-Indies.

If it is assumed—as I do—that the diagnosis of the heart specialist, who thoroughly examined the patient, was correct, how can this all-round recovery, at least as regards function, be explained? For that I should like to cite Mozer (6). He discussed the anastomoses between the right and the left coronary arteries of the heart, which are apparently not, as we learned formerly, end-arteries. „Those anastomoses are no anatomic curiosities; they develop progressively with an infarct in one of the branches, by haemodynamic over-pressure from the art. coronaria. By these anastomoses the long living of some patients suffering from heart-diseases can be explained.” So far Mozer. Also the recovery of my patient I. and of several suchlike patients, whom I cured with hypnosis, I want to explain in the same way.

¹ Corrector's remark: Now she has been well more than 3 years.

By relating the above cases, which represent a rather casual handful of a great number of suchlike patients, I want to lay special stress on the unbreakable connection of body and soul, a connection that makes us wonder in every fresh case. When every medical practitioner will always remember this unity, many serious patients, even those who seem to be past recovery, will possibly be cured.

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CONTRIBUTION A L'ÉTUDE DE LA MALADIE FRIEDREICH

Par

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C'est un fait reconnu que la maladie de *Friedreich* est un représentant caractéristique des affections nerveuses héréditaires. Une communication toute récente de *Dorothy S. Russel*, présentant quelques cas de myocardite interstitielle chronique (1946) d'origine toxique, est d'autant plus surprenante. Elle pose la question des dégénération du myocarde et du système nerveux comme une entité d'origine commune. Notre rapport présente cinq observations relatives à la maladie de *Friedreich*, dont l'une manifeste une lésion légère, une autre une atteinte plus prononcée du myocarde.

1/ Sujet mâle, 26 ans. Agé d'un an et demi, il a fait une grippe espagnole. L'un de ses frères a le pied remarquablement raccourci, avec convexité marquée du dos du pied. L'état morbide a débuté en 1937 par des vertiges, difficultés de la marche. Pupilles et nerfs normaux, pas de nystagmus. Les réflexes brachiaux sont déclenchables. Réflexes patellaires et achilléens absents des deux côtés. Ni réflexes pathologiques, ni clonus. Du côté g. : tremblement intentionnel léger, — ataxie prononcée à l'épreuve genou-talon. Pied bot accusé bilatéral (voir fig. 1.). A la main g., interosseux des doigts II, III, IV, atrophiés. Démarche nettement atactique, de caractère cérébelleux. Autre test : Bordet-WA négatif pour le sang et le liquide CR. L'état est, 6 mois plus tard, stationnaire.

2/ Sujet mâle, 23 ans. Faiblesse de la vue et difficultés de la marche, remontant à l'enfance. Maux de tête fréquents, vertiges, incertitude statique, démarche titubante. Pupilles et nerfs craniens normaux. Nystagme horizontal vers la droite. — Réflexes brachiaux et abdominaux déclenchables, réflexes patellaires diminués des 2 côtés. Réflexes achilléens manquent. Signe de Babinski, et pied bot bilatéral, (voir fig. 2.) membres inférieurs parétiques, hypotonie.

Force musculaire des extrémités supérieures intacte. Les auriculaires des 2 mains contractés et fléchis/contracture *Dupuytren* (voir fig. 3.) Celle-ci est de caractère familial. Démarche : atactique-parétique. Hypermétrie à l'épreuve genou-talon. Sang et liquide CR Bordet-Wa négatifs. Atrophie du nerf optique bilatéral.



Fig. 1.

3/ Sujet féminin, 17 ans. La mère de la malade est morte à 31 ans dans un coma diabétique. La maladie du sujet remonte à 7 ans. La démarche est devenue hésitante, chancelante. Soignée en 1940 et 43 à l'Hôpital de la Croix Rouge, amélioration, depuis près d'un an le sujet est incapable de marcher. Vertiges fréquents, ni douleurs, ni nausées. — Cyphoscoliose dorsale à convexité droite. Nerfs craniens normaux. Aucun nystagmus. Les réflexes brachiaux, patellaires et achilléens sont déficients. Signe de Babinski bilatéral plus accusé à g. Musculature hypotonique, ataxie très prononcée à l'épreuve nez-doigt, ainsi qu'à celle du genou — talon. Démarche : quelques pas titubants en s'appuyant fortement des deux côtés. Ataxie prononcée

du torse et des jambes, l'attitude verticale est impossible à maintenir, oscillations globales, chute en arrière. Les jambes étendues ne s'élèvent que jusqu'à 50—60 degrés. Force musculaire de la main dr.: 6 kg., de la main g : 12 kg. A droite : musculature atrophiée de l'hypothénar. La parole est scandée, difficile à comprendre. Pas d'anomalies sen-



Fig. 2.

sitives. Psychiquement le développement correspond au niveau d'un enfant de 7—8 ans. Incapacité pour les plus simples problèmes d'arithmétique. Fond d'œil normal, Hypesthésie bilatérale vestibulaire et hypesthésie cochléaire droite. Réactions du sang, du liquide CR négatives. EKG: rythme sinusal, fréquence à 85. Dextrogramme. T₁ bas, positif, T_{2—3} négatifs, ST oblique, ST 2—3 déprimés, arrondis (voir fig. 4). Lésion typique du myocarde.

4/ Sujet mâle, 35 ans. Le frère du sujet, comme lui-même, ont un pied bot. Il y a environ 15 ans, la paupière droite du malade s'est abaissée en moins de 2—3 jours. Il ne pouvait ouvrir l'œil qu'à l'aide de sa main. Bordet-Wa négative. La maladie a été rapidement enrayée par un traitement de B 1. Un an plus tard; affaiblissement successif du pied dr., puis g., avec incapacité de se hausser sur la pointe des pieds. Fléchissement du pied en marchant. Amélioration

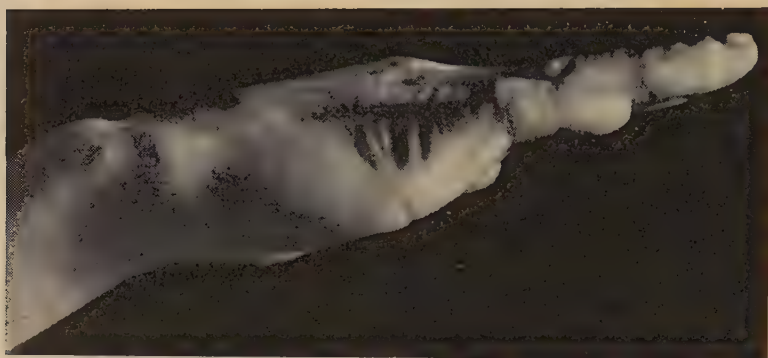


Fig. 3.

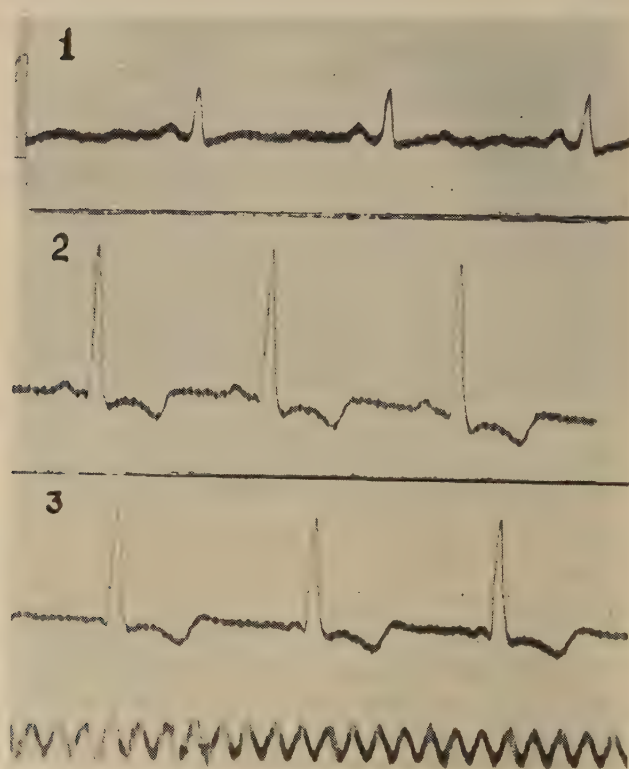


Fig. 4.

passagère suivie, deux ans plus tard, d'une faiblesse plus accentuée, se portant aussi sur les main. Diplopie. Une seconde amélioration plus faible que la première. Depuis un an environ, l'état s'aggrave graduellement.

Observation: anisocorie légère, les deux pupilles irrégulières, réflexes pupillaires amoindris à la lumière. Nystagmus horizontal à petites ondes vers la gauche. Parésie faciale centrale dr. Le voile du palais reste mobile, la langue montre des fibrillations musculaires prononcées. Réflexe brachial plus prompt à g., déclenchable à dr.

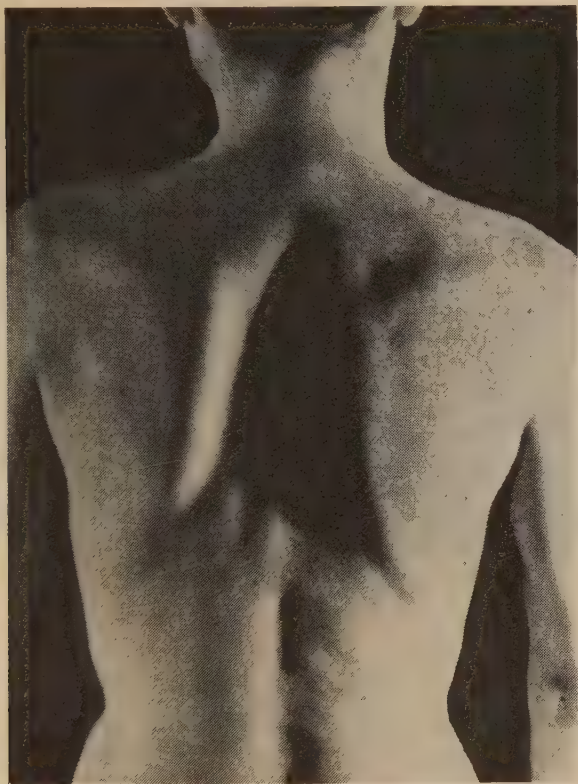


Fig. 5.

Réflexes patellaires diminués des deux côtes, réflexes achilléens abolis. Ni réflexes pathologiques, ni clonus. La musculature est assez faiblement développée, atrophie moyenne bilatérale des épaules et des homoplates, scapulae alatae peu accusées (voir fig. 5.). Atrophie musculaire distincte, bilatérale, de l'avant-bras, thénar, hypothenar et des interosseux, atrophie musculaire grave des membres inférieurs (voir fig. 6. et 7.). Pied bot bilatéral (voir fig. 8.). Fibrillations plus fréquentes dans la musculature des deux deltas, plus rare dans celle de l'homoplate dr. Force manuelle: 30 kg à dr., 10 kg. à g. Steppage plus prononcé à droite. Le sujet marche les jambes écartées, les genoux

soulevés de façon incertaine. Signe de Barré nég. Pas d'anomalie sensitive. Psychisme : indemne. Liquide CR : albumine 10 mgr %, nombre cellulaire Ø, Pándy-Nonne 1—1 + pos. Takata : + Bordet-Wa nég., la courbe colloïdale du sang (benzoë) également normale. Fond d'oeil indemne des deux côtés. Hypesthésie vestibulaire discrète bilatérale.



Fig. 6.

5/ Sujet mâle, 45 ans. Nystagmus, pied difforme depuis l'enfance. A la trentaine, ses jambes ont perdu leur ressort, sa démarche s'est faite difficile. A 35 ans, résultat sanguin positif. Sur trois frères, l'un a les deux pieds creux, le droit plus prononcé, orteils contractés, (maladie de *Friedreich* rudimentaire). Observation : anisocorie, réaction pupillaire ralentie par égard à lumière, pâpilles blanches, atrophifiées, nystagmus rotatoire, ataxie cérébelleuse, pied bot typique. Réflexes patellaires et achilléens abolis, ceux de l'abdomen, de la peau et des muscles déclenchables (réflexe de Guillain). — Du côté dr., signe de Babinski ébauché, Romberg positif, asynergie cérébelleuse. A g. adiadochokinèse prononcée. Fonctions sensitives, normales, excepté l'absence des sensations vibratoires aux membres inférieurs et aux os iliaques. La parole est trainante, scandée. .Pas d'altérations psychiques. Sang, liquide CR : Bordet-Wa négative. Liquide CR : albumine totale 30 mgr %, taux cellulaire $\frac{2}{3}$, Pándy +, les autres réactions colloïdales et globulaires normales. EKG : tachycardie sinusique, laevogramme, onde T aplatie : lésion légère du myocarde.

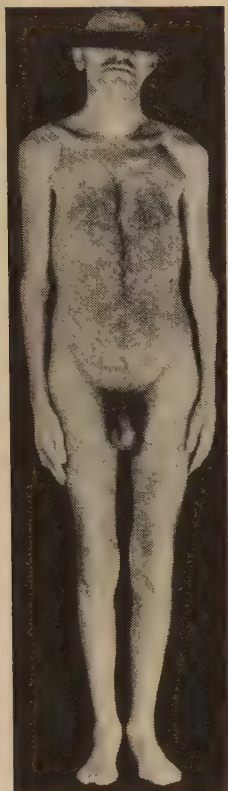


Fig. 7.



Fig. 8.

DISCUSSION

Quatre de nos sujets — 1, 2, 3, 5, — présentent une pure forme de l'hérédo-ataxie spinale, ou maladie de *Friedreich*. Le diagnostic s'appuie — premièrement sur la constatation du pied bot dans chaque cas, — puis sur la présence conjointe au moins de deux symptômes cardinaux des trois qui distinguent cet état soit : nystagmus spontané, aréfléxie et ataxie stato-locomotrice. Nous avons noté l'aréfléxie, ou une diminution considérable des réflexes patellaires et achilléens dans 3 de nos cas. L'ataxie n'était pas moins prononcée. Le nystagmus était évident dans les cas No 2 et 5, ainsi que dans le No 4, sur lequel nous reviendrons plus tard. Il était absent chez deux malades. Ceci n'exclut nullement la maladie de *Friedreich*, vu que le nystagmus manque dans 30 % des cas, notamment au début de la maladie. En conséquence, et en tenant compte des données anamnestiques, il semble raisonnable d'estimer que le mal a duré environ 10 ans chez ces deux malades, 15—20 chez les autres cas cités.

Le signe de Babinski a été constaté dans les cas 2, 3, 4. 5, et manque dans le cas No 1. C'est pourquoi nous le classifions, d'après *Mollaret*, parmi les formes frustes de la maladie de *Friedreich*. Ce cas, ainsi que le No 3, manifeste encore d'autres particularités intéressantes : le premier présente une atrophie nettement prononcée dans les interosseux de la main, le second un phénomène identique à l'hypo-thénar droit. D'après *Hallervorden*, l'atrophie musculaire s'allie bien plus souvent accessoirement à la maladie de *Friedreich* que les communications ressortissantes ne le donnent à penser. Elle se manifeste le plus souvent dans les interosseux de la main et dans la musculature scapulaire et péronnée. *Wilson* décrit chez un malade l'atrophie des interosseux de la main gauche, couplée à celle de la jambe droite. Vu que ces atrophies manuelles étaient unilatérales, donc isolées chez tous nos sujets, nous les classons parmi les „formes cliniques spéciales“ (*Van Bogaert*). Des observations-contrôles seront chargées de préciser si cette atrophie musculaire est bien simplement un symptôme accessoire, ou plutôt une complication, -voir notre cas 4, qui impliquerait l'incidence de la maladie de *Friedreich* alliée à d'autres maladies hérédo-dégénératives.

Par rapport aux nerfs craniens nous avons constaté l'anisocorie et des pupilles irrégulières, aréfléxie à la lumière dans les cas 4 et 5. Le cas 5 présente une atrophie du nerf optique. Quoique ce fait ait été fréquemment noté — voir *Londe* — il s'agit probablement dans ce cas d'une infection syphilitique. Cette supposition s'applique aussi à nos malades, puisque l'anamnèse découvre chez l'un une ptose de

la paupière droite, 15 ans plus tôt, guérie par un traitement anti-vénérien, tandis que le sang de l'autre était positif à l'âge de 35 ans. Il est vrai que nos tests actuels ont démontré la négativité du sang, mais le Pándy-Nonne du liquide CR était positif. La parésie faciale centrale ne rentre pas dans le cadre du syndrome de *Friedreich* et plaide pour l'hypothèse vénérienne.

Nous n'avons trouvé aucune trace des symptômes se rapportant aux nerfs cérébraux notés dans la littérature, tels que : parésie du nerf VI. III. ou du regard. *Marie-Thiers* et surtout *Guillain* ont maintes fois souligné la lésion fréquente du système vestibulaire. *Mollaret* a expliqué l'hypesthésie vestibulaire par la dégénération du nerf. Nous avons constaté dans deux cas ; hypesthésies vestibulaires bilatérales (3 et 4) —, une fois lésion vestibulaire centrale bilatérale — (5) —, et en outre une hypesthésie cochléaire droite, également illustrée par le sujet No 3. Mention est faite d'une lésion de la branche cochléaire, ou surdité, — dans nombre de communications (*Lichtenstein, Knorr, Frey, Curtius* etc.). *Alexander* et *Ono* ont même démontré anatomiquement l'atrophie du nerf cochléaire et des cellules nerveuses du ganglion spiral.

Guillain et collab. ont noté en rapport avec la maladie de *Friedreich* un trouble du rythme cardiaque, dont ils rendent responsable la fonction altérée du nerf pneumogastrique bulbaire. *Guillain* trouve ainsi, dans un de ses cas une raréfaction cellulaire dans tous les noyaux de la base du 4^{ème} ventricule. *Sigwald Refsum* note dans deux familles atteintes d'hérédoopathie atactique deux cas d'anoxie myocardique, trois tachycardies sinusales, un trouble discret de la conduite atrio-ventriculaire. Malgré nos recherches spéciales et les électrocardiogrammes pris avec soin, nous n'avons pas rencontré une seule de ces anomalies rythmiques. Le cas No 4 manifestait par contre une lésion prononcée, le cas No 5 une lésion légère du myocarde.

Le réaction myasthénique d'après *Jolly* a été notée dans plusieurs cas. Nous n'avons toutefois pas réussi à la démontrer. Nous acceptons donc l'avis de *Bing* qui classe l'observation de *Kramer, Maybarduk* parmi les complications.

Mollaret évalue l'occurrence des anomalies psychiques dans la maladie de *Friedreich* à 25 %. L'imbécillité constitutionnelle est fréquente, et des formes plus graves d'idiotie mongoloïde ont une certaine incidence.

Parmi nos cas, c'est le No 3 — jeune fille de 17 ans, — qui présentait des anomalies de développement intellectuel. Ses facultés correspondaient à celles d'un enfant de 7-8 ans et nous avons trouvé une mémoire défectueuse, absence de jugement, attitude infantile graves.

Par contre, trois autres sujets étaient psychiquement normaux. Concernant les troubles mentaux, les uns admettent leur simple coïncidence, d'autres les considèrent comme liés à des lésions corticales.

La réaction de Pándy-Nonne de notre premier cas se chiffre par + + + celle de Takata-Ara par + +. Vu la présence de sang mêlé au



Fig. 9.

liquide CR, il est impossible d'évaluer exactement cette réaction. Il se peut qu'il s'agisse dans ce cas d'une augmentation lymphocytaire relative à l'état morbide, ainsi que *Barjon*, *Cade* et d'autres l'ont affirmé. *Wilson* met en doute l'importance de ce fait, *Vercelli*, *Guillain*, *Mollaret*, rapportent une altération nettement focale non syphilitique! Nous rappelons la réaction Pándy-Nonne et Takata-Ara faiblement positive des cas 4,5 (taux : +) parce que l'anamnèse de ces malades comporte des données vénériennes. Ces cas, atteints de la maladie de *Friedreich* forment donc un groupe dans lequel le liquide CR décele les traces d'une syphilis antérieure (*Claude-Rouillard*, *Benelli*, *Zucarelli*, *Forteau-Donati*, *Dawidenkow*), *Van Bogaert* considère ces infections vénériennes comme des coïncidences.

Le pied bot est une anomalie que nous retrouvons dans chacun de nos cas. Cette anomalie n'entraîne aucune déformation osseuse. L'on en explique l'origine par la contracture, respectivement l'atrophie, de certains muscles du pied, spécialement du m. *tibialis anticus* et *posticus*. *Bing* note chez un malade constamment alité la disparition du pied de *Friedreich*. Nous avons fait des observations similaires par rapport à notre sujet No 3., incapable de marcher (voir fig. 9) *Van Bogaert* trouve d'ailleurs au pied creux le même importance qu'au pied bot. Une autre anomalie la cyphoscoliose citée par *Mollaret* pour 2/3 des cas, par *Thomas-Barret* pour 83 %, n'a été confirmée que par une seule de nos observations (le No 5).

La parole difficile, scandée, n'était manifeste que dans notre cas 3, moindre dans le 5. Il semble que ce symptôme n'ait pas l'importance diagnostique qui lui était accordée anciennement, (*Bing, Dejerine, Thomas*).

Les désordres sensitifs ont été soulignés par *Kroll*, il y a déjà 35 ans, sans avoir atteint dans le diagnostic clinique la place qui leur serait due. La cause en serait, que ces examens nécessitent un procédé spécial : 30-40 milliampères de courant galvanique sont indispensables pour établir systématiquement le trouble de la douleur et sensibilité profonde. L'un de ses malades était tellement dépourvu de cette dernière, qu'il ne « retrouvait pas sa main » dans l'obscurité. L'auteur décrit en outre un sens retardé de la douleur et de l'hyperpathie. *Egedy-Klimes* constatent l'hyperpathie dans une famille atteinte de la maladie de *Friedreich*. Nous avons noté pour le cas 3 des troubles sensitifs profonds, pour le 5 une anesthésie vibratoire.

En parcourant les symptômes cliniques de nos cas 1, 2, 3, 5 nous pouvons affirmer que tous manifestent une forme avancée de l'ataxie de *Friedreich*. Le premier stade, soit le syndrome purement cérébelleux de caractère statique y est dépassé; nous distinguons des symptômes d'aréflexie (deuxième phase), et de paraplégie avec signe de Babinski (troisième phase).

Nous faisons une place à part au syndrome de notre sujet 4 vu l'intérêt spécial qu'il présente.

Le résumé des symptômes nous permet de constater que le sujet — mâle, âgé de 35 ans — marche avec difficulté depuis 14 ans. Voici 12 ans que ses mains sont faibles. La musculature des extrémités supérieures et inférieures, ainsi que les interosseux de la mains ont atrophiés. Atrophie dégénérative dans la musculature scapulaire, fibrillations.

Cela correspondrait à une sclérose latérale amyotrophique. Par contre, le réflexe achilléen, l'ataxie, l'indemnité du psychisme et le pied creux constituent le syndrome de la maladie de *Friedreich*.

Ce malade manifeste donc une sclérose latérale amyotrophique alliée à la maladie de *Friedreich*, que *Van Bogaert* qualifie de « forme amyotrophique ». *Bing* et *Werthemann* notent chacun un cas d'atrophie musculaire progressive, *Kollarits* un cas compliqué de chorée de *Huntington*, *De Morsier* note une paralysie bulbaire qui se joint à l'hérédodystaxie. Un malade de *Marburg-Riese* complète le syndrome par un tremblement de la tête, l'amyotrophie des extrémités inférieures et par les troubles psychiques. *Van Bogaert-Moreau*, *Biemond*, *Roth*, notent le développement d'une ataxie de *Friedreich* et d'une atrophie musculaire neurale dans la même famille. Deux familles norvégiennes de *Sigwald Refsum* méritent notre attention; il y note une héméralopie, une rétinite pigmentée, une polynévrite, de l'ataxie des symptômes cérébelleux. Il rattache ce syndrome à l'hérédodystaxie et à l'amyotrophie neurale. Dans notre cas, le syndrome atrophique est atypique, vu que l'atrophie musculaire a premièrement attaqué les extrémités inférieures pour ne passer que plus tard aux extrémités supérieures, mais aussi du fait que 14 ans de cet état n'ont pas entraîné de symptômes bulbares.

Des traits hérédofamiliaux apparaissent dans 4 de nos 5 cas : 1, 4, 5 ont chacun un frère affligé du pied-*Friedreich*, le 2^{ème} malade a une contracture *Dupuytren* avec l'auriculaire contracté. Cette dernière question a été traitée en détail par *Orbán*. Il a trouvé ce symptôme dans trois membres féminins d'une famille atteinte de *Friedreich*. *Orbán* se rallie à l'interprétation de *Schaffer*, il envisage l'anomalie comme une hérédodégénération mésodermale. Il ajoute cette observation remarquable que l'ataxie *Friedreich* est une récessive héréditaire, la contracture *Dupuytren* par contre une dominante héréditaire.

Un diagnostic différentiel net entre la maladie de *Friedreich* et l'hérédodystaxie cérébelleuse de *Marie* est difficile, vu l'atypie fréquente des deux états et leurs formes transitoires.

L'atrophie optique, la paralysie du nerf oculomoteur et le tremblement intentionnel appuient généralement l'hypothèse de la forme cérébelleuse.

Ces difficultés expliquent la nomenclature commune donnée aux deux formes : « les hérédodystaxies ». Cette tendance d'unification prend son point de départ dans les communications de *Bing* (1905). Ses adeptes : *Hanhart*, *Mollaret*, *Jaspy*, *Van Bogaert* et même *Wette* et *Rosenhagen* parlent d'hérédodégénérescence spino-ponto cérébelleuse. Par contre, *Kalinowski* et *Dawidenkow* persistent à y voir des syndromes distincts. Ces divergences soulignent le fait que l'étude des maladies nerveuses héréditaires exige une révision complète, tenant compte des investigations modernes.

La communication citée plus haut de *Dorothy S. Russel* vise ce but : elle y énumère 4 cas d'ataxie *Friedreich* compliqués de myocardite interstitielle chronique, 3 cas dans lesquels l'hypertrophie cardiaque est nettement prononcée. Les noyaux du nerf pneumogastrique ne décelaient aucune altération histologique. Ce sont surtout les savants français qui ont étudié la lésion du myocarde (*Pic-Bonnamour, Guilain-Mollaret, Loiseau*) certains d'entre eux en accusent l'affection du noyau pneumogastrique. *Van Bogaert* y voit l'expression de troubles végétatifs. D'autres auteurs — *Lannois-Parot, Lambrior*, — rendent le facteur toxique responsable des altérations myocardiques et neurales. Les données de *Russel* semblent soutenir cette dernière hypothèse, ce qui l'incite à admettre que les lésions cardiaques et neurales de l'ataxie *Friedreich* sont dues à un même agent.

Ainsi le facteur toxique comme agent supposé *commun* des deux altérations nous oblige à continuer l'étude de l'hérédité dans cette maladie. Il est évident qu'une fois sa persistance systématiquement démontrée, il ne saurait plus être question que d'une prédisposition héréditaire, pathologiquement déclenchée par le facteur exogène.

Au cours de nos observations nous avons rencontré une myocardite prononcée, une autre discrète, sur un total de 5 cas. Par conséquent, nos expériences cliniques ne confirment pas, ou ne confirment que partiellement, la constatation pathologique de *Russel*. Nous sommes cependant d'avis que les données histopathologiques et anatomopathologiques de *Russel* méritent la plus sérieuse attention. Les recherches futures seront appelées à éclaircir ce problème.

RESUME

5 observations cliniques de la maladie de *Friedreich* : 4 sujets mâles, 1 fem., — quatre cas « purs » et un combiné de la sclérose lat. amyotrophique. Traits hérédo-familiaux dans 4 cas : 3 malades ont un frère affligé de pied bot, l'un, ainsi que sa famille, manifeste la contracture auriculaire de *Dupuytren*. Le cas No. 3 présente une lésion myocardique accusée, le No. 5 une lésion semblable, discrète. Celles-ci sont absentes chez les autres sujets. La présomption qu'un agent toxique commun est responsable des lésions myocardique et neurales doit encore faire ses preuves cliniques et pathologiques.

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NEUROPATHOLOGIE DES INSTITUTS BUNGE, ANTWERPEN
(DIREKTOR: DR. LUDO VAN BOGAERT)

UEBER EINE VESTIBULO-CEREBELLÄRE ENTWICKLUNGSHEMMUNG IM RAHMEN AUSGEDEHNTER OSTEO-NEURALER DYSGENESIEN

Von

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DISKUSSION

Es handelt sich um einen Fall von ausgedehnter Hypoplasie des Zentralnervensystems, welcher wir wegen der im Vordergrund stehenden Entwicklungshemmung des Kleinhirns, besonders des Neo-Cerebellums und z. T. des Palaeo-Cerebellums mit ihren afferenten und efferenten Bahnen der Gruppe der *cerebellären Hypogenesien* zuteilen. Unser Fall ist eng mit den symmetrischen cerebellären Agenesien, die durch Entwicklungshemmung nach der Koaleszenz der rhomboiden Lippen und der Ausbildung der Wurmknospen bedingt sind, verwandt. Es weist lediglich einen rudimentären Vermis, unterentwickelte Floculi mit corticalen architektonischen Alterationen und Hypoplasie der Kleinhirnantile des Hirnstammes auf. Einige ähnliche Fälle wurden bereits beschrieben (*Zingerlé* und *Anton*, *Ferrier* und *Shuttleworth*, *Brun*, *Baker* und *Graves*). In unserer Beobachtung muss, wie bereits in den von den obenerwähnten Autoren beschriebenen Fällen der *teratogene Determinationspunkt im 3. Foetalmonat liegen*. Wir weisen jedoch darauf hin, dass die Ursache der Entwicklungshemmung noch in späteren Monaten gewirkt hat. Wir haben nämlich eine fast vollständige Aplasie der unteren Oliven, die sich im 3. Monat entwickeln, und eine Entwicklungsalteration des Nucleus dentatus, dessen Ausbildung später erfolgt, gefunden. Weiter zeigen sich Purkinje'sche

Zellen ohne irgendwelche Veränderungen. Die Masse des Kleinhirns entsprechen den Resultaten der Arbeit von *Scammon* und *Dunn* („On the growth of the human cerebellum in early life“), was auch unserer Auffassung entspricht, nämlich dass dieses Kleinhirn sich bis zum 6. Monat weiter entwickelt hat.

Die *Ursache der beschriebenen Entwicklungshemmung* ist nicht offensichtlich. Nach der schönen Arbeit von *Brun* über cerebelläre Dysgenesien hat man allgemein seine Klassifikation anerkannt, welche einerseits sekundäre Entwicklungsstörungen (entzündliche, vaskuläre oder toxische Erkrankungen) und andererseits eine primitive endogene Alteration annimmt. Die letztere sollte als diffus toxisch aufgefasst werden. *Brodal* hat aber in der Diskussion eines ähnlichen Falles die Meinung geäußert, dass die *Brun'sche* toxische Auffassung der Noxe zu eng sei. Doch scheint es uns, dass die Hypothese von *Brun* durch die neueren Arbeiten von *Töndury* gestützt wird. *Töndury*, welcher die Wirkungsweise der Gene aus die embryonale Entwicklung studiert hat, vertritt die Ansicht, dass die Differenzierungsvorgänge durch genische, hemmende Stoffe beeinflusst werden. Diese hemmenden Stoffe sind gleicher Natur wie diejenigen, die — wie zahlreiche biologische Experimente gezeigt haben — das Wachstum fördern. In unserem Falle liegt die Annahme *Brun's* in der Diskussion seiner zahlreichen Fälle von Kleinhirnhypoplasien und Dysgenesien am nächsten, dass auch bei partiellen tektonischen Dysgenesien die Ursache letzten Endes in einer allgemeinen „toxischen“ Schädigung zu suchen sei.

Die endogene oder exogene Natur dieser Schädigung ist uns nicht bekannt, da keine spezifischen oder charakteristischen Bilder zum Vorschein kommen. Eine Erkrankung der Mutter in graviditate (Rubellen, Grippe und dergl.) konnte ebenfalls nicht eruiert werden. Die Hirnveränderungen treten in unserem Falle familiär auf (Mikrencephalie) und sind mit einer angeborenen Hyperostose und weiteren Körpermissbildung vergesellschaftet. Diese Häufung von Missbildungen spricht eher für ein endogenes Vitium primae formationis.

Unsere Beobachtung stellt uns vor mehrere schwierige Probleme, welche bis jetzt die Aufmerksamkeit der Autoren nur wenig auf sich gezogen haben. Wir möchten zuerst auf die Zusammenhänge zwischen den *Entwicklungsstörungen im Zentralnervensystem und den diffusen Knochenveränderungen hinweisen*. *Koszewski* hat nämlich im gleichen Fall über eine vergesellschaftete angeborene, diffus generalisierte Hyperostose berichtet.

Die frühzeitige Hemmung des Knochenumbaus ist für diese Veränderungen verantwortlich, die zu einem Darniederliegen des Knochen-

gewebsaubbaustadiums und zu einem relativen Ueberwiegen des Anbaues führt. Diese Knochenkrankheit grenzte der Autor gegenüber der Marmorknochenkrankheit von *Albers-Schönberg* ab. Das Studium des Gehirns ergibt keine befriedigende Erklärung für die generalisierte angeborene Hyperostose.

Wir fanden im Schrifttum keine einzige Beobachtung, wo nervöse Verbildungen von einer bedeutenden und generalisierten Störung der Osteogenese, wie in unserem Fall, begleitet werden. Meistens erwähnen die Autoren das Knochensystem überhaupt nicht. *Tintenmann* ist der einzige, der es in seinem Fall untersucht und normal befunden hat (33-jähriger Mann im teilweiser Kleinhirnaplasie und frontaler Meningo-Encephalocele).

Zolotowa hat eine Arthrogryposis der vier Extremitäten, verbunden mit ausgedehnter cerebellärer Missbildung beschrieben (6-tägiges heredo-luetisches Kind). Sie hält diese Skelettmissbildungen für eine Folge ausgedehnter und diffuser Ganglienzellveränderungen der Vorderhörner. Am häufigsten sind aber nur lokale Missbildungen des Schädels und der Wirbelsäule erwähnt, die mit Entwicklungsstörungen des Zentralnervensystems verbunden sind (*Huppert, Jacob, Priestley, Fischer, Anton und Zingerlé, Otto* usw.). Solche Fälle sind durch die gegenseitige Wirkung der beiden Systeme zu verstehen und sprechen nicht für eine allgemeine und diffuse Knochenbildungsstörung.

Unser Fall scheint also neuartig, da er sich durch eine ausgedehnte Missbildung des Zentralnervensystems auszeichnet, verbunden mit einer kongenitalen Hyperostosis eines seltenen Typus. Infolgedessen sollte man annehmen, dass es sich bei dieser Erkrankungsform um voneinander unabhängige Leiden handelt. Man könnte eventuell — die Einteilung von *Brun* weiter ausdehnend — die Knochenveränderungen als primäre korrelative Veränderungen des Skeletts auffassen. Die angenommene Noxe hätte gleichzeitig hemmend auf das Zentralnervensystem und auf das Knochensystem gewirkt, was die Hypothese von *Otto* in seiner Diskussion der Schädelveränderungen mit Dysgenesen des Kleinhirns bestätigen würde.

Brun beschreibt zwei Typen von relativen Veränderungen bei den cerebellären Entwicklungsstörungen:

1. die „primären korrelativen Entwicklungshemmungen“; dieselbe Noxe wirkt gleichzeitig auf andere Sektoren des Zentralnervensystems und auf das Kleinhirn.
2. „Sekundäre korrelative Entwicklungshemmungen“, in welchen die extracerebellären Störungen nicht direkt durch die Noxe erklärbar sind. Sie sind als sekundär aufzufassen durch Regression der morphologischen Stimulation, welche normalerweise durch das Kleinhirn auf die abhängigen Strukturen (Kleinhirnanteile) erfolgt.

DAS VERHALTEN DES VESTIBULÄREN SYSTEMES IN DIESEM DYSGENETISCHEN RAHMEN

Im Laufe unserer histologischen Beschreibung haben wir kurz mitgeteilt, dass die vestibulären Kerne am hypoplastischen Vorgang teilnehmen.

Von der lateralen Kernsäule (Area fasciculata, IAK, *Fuse*) sind nur einzelne Elemente auffindbar (tractus spinalis vestibularis und Roller'scher Kern), welche normalerweise bis auf das Niveau der maximalen Ausdehnung der unteren Oliven hinabreichen sollten. In dieser Zone liegen einzelne, im Gliagewebe verstreute, deutlich unterentwickelte Elemente. Dagegen ist der Deiter'sche Kern besser ausgebildet, wenn auch in seinen Ganglienelementen unterentwickelt. Wir finden seine Ganglienzellen im dorso-lateralen Gebiet des IV. Ventrikels. Die Ganglienzellen sind kleiner als normal, mit dunklem Kern und von rundlicher Gestalt. Sie reichen bis zum Quintuskern, von dem sie schlecht abgegrenzt sind. Auf diesem Niveau gewinnt man den Eindruck einer Zellarmut mit zahlreichen gliaähnlichen Kernen (Bildungsmaterial) und hypoplastischen Elementen. Die Uebergangszone zwischen dem Deiter'schen Kern und dem Nucleus triangularis ist sehr deutlich, da die Zellen in diesem Gebiet besonders spärlich sind. Was den Nucleus Bechterew anbetrifft, so sind in seinem Areal nur einzelne, weit verstreute Ganglienzellen sichtbar. Die Elemente des Bechterewkernes reichen nicht weiter oralwärts als der Quintuskern. Vom ganzen vestibulären System ist der Nucleus triangularis am besten entwickelt, mit zahlreichen, gut ausgebildeten Ganglienzellen. Die übrigen Anteile des vestibulären Systems können wir nicht beurteilen.

Zusammengefasst ist die Lateralkernsäule (I.A.K.) auffallend stark in ihrer Ausdehnung und Entwicklung gehemmt, dagegen ist die mediale Säule gut ausgebildet. Infolge technischer Schwierigkeiten ist es uns nicht möglich, die vestibulären Bahnen und ihre Zusammenhänge mit den hypoplastischen Kleinhirnelementen und Anteilen zu prüfen.

Die meisten der von uns zusammengestellten Fälle von symmetrischer und asymmetrischer Kleinhirnagenesie enthalten keine Angabe über das Verhalten des vestibulären Systems. Wir haben lediglich acht solche Beobachtungen gefunden, in denen dieses erwähnt ist. Unter diesen weisen die folgenden Fälle hinsichtlich der vestibulären Kerne einen normalen Befund auf:

Krause (1929) berichtet über eine endogene Entwicklungshemmung des Kleinhirns, besonders des Neocerebellum, dessen teratogener Determinationspunkt im späten 3. Foetalmonat liegt. Die Zellen des N. Deiteri, des N. triangularis und angularis, des tuberculum acusticus sind in ausreichendem Masse vorhanden. In einer Reihe von Schnitten war es möglich, Fasern aus dem Flocculus bis in die Gegend des Zellareals des N. triangularis zu verfolgen. *Robert S. Dow* (1940) hat eine partielle Agenesie des Cerebellum bei jungen Hunden studiert. Aus diesen Beobachtungen (Determinationsperiode sollte diejenige einer neocerebellären Apla-

sie mit palaeocerebellären Komponenten sein) geht hervor, dass das vestibuläre System normal befunden wurde. *Rubinstein* und *Freeman* (1940) haben bei einem 71-jährigen Patienten mit neocerebellärer Agenesie beobachtet, dass die vestibulären Kerne und Verbindungen nicht alteriert waren. Zuletzt hat *Sahs* (1941) eine congenitale Aplasie des Kleinhirnwurms bei einem 16-jährigen Knaben mit normalem vestibulärem Befund beschrieben.

Im Gegensatz dazu haben verschiedene Autoren über atypische Befunde im vestibulären System bei cerebellären Agenesien berichtet, ohne dass diese Beobachtungen grosse Aufmerksamkeit erweckten.

Anton (1903) beschreibt bei einem 6-jährigen Idioten mit Kleinhirnaplasie eine Reduktion des caudalen Anteiles des N. Deiteri (kleinzelliger Anteil); die übrigen vestibulären Kerne, auf der einen Seite ausgeprägter, liegen in einem sklerotischen Gewebe. *Brun* (1918) beschreibt in seinem Fall I (Aplasia neocerebellaris) einen Ausfall an Substantia molecularis und an kleinen Nervenzellen innerhalb der lateralen I.A.K.-Geflechte, sowie — in kleinerem Ausmass — im Nucleus triangularis, was unserem eigenen Befund gut entspricht. Es ist hier hinzuzufügen, dass nach unserer Ansicht der Fall von *Brun* unserem eigenen am ehesten entspricht. Der teratogene Determinationspunkt kann in beiden Fällen in dieselbe Foetalperiode verlegt werden. In seinem Fall von palaeo-cerebellärer Aplasie hat *Lyssenkow* (1931) den oberen Anteil des Nucleus triangularis als aplastisch und sklerotisch beschrieben. In dieser Beobachtung werden die aufsteigenden vestibulären Fasern zu den fehlenden Kleinhirnelementen vermisst. Endlich beschreibt *Castrillon* (1933) in seiner Betrachtung (partielle palaeo-cerebelläre Agenesie einen in der Form veränderten nucleus triangularis).

Diese verschiedenen Beobachtungen zeigen, dass das vestibuläre System nur in Fällen von cerebellären Agenesien mit frühzeitiger Hemmungsnoxe verändert wird. Es ist offensichtlich, dass die vestibuläre Entwicklungsstörung nicht direkt von der alleinigen Ausbildungshemmung des Neo-Cerebellums oder des Palaeo-Cerebellums abhängt. In der Tat finden wir Fälle, in denen die neocerebelläre Agenesie keine Alteration der vestibulären Kerne und Bahnen aufweist. Die angenommene Noxe wirkt nur auf die Kerne, wenn sie in einer bestimmten Determinationsperiode derselben auftritt, d. h. am Ende des 2. und am Anfang des 3. Foetalmonats. Wir nehmen an, dass es sich hier um eine primäre korrelative Veränderung handelt. Wir möchten unterstreichen, dass die vestibulären Veränderungen im Gebiet der lateralen Kernsäule ausgeprägter sind, nicht nur in unserem eigenen Falle, sondern auch in allen anderen hier zusammengestellten Beobachtungen. Unser histologisches Material reicht nicht aus, um die afferenten und efferenten vestibulären Bahnen eingehend zu beschreiben, was eine genauere Interpretation schwierig macht. Aus diesem Grunde ist nur eine summarische Beschreibung gerechtfertigt, welche trotzdem neue Gesichtspunkte in das Studium der cerebellären Dysgenesien bringt.

ZUSAMMENFASSUNG

Es wird über einen seltenen Fall von Entwicklungshemmung des ganzen Kleinhirns, besonders der neo-cerebellären Anteile, berichtet. Im Vordergrund der zahlreichen Missbildungen des Zentralnervensystems stehen die symmetrischen Veränderungen des Kleinhirns und der zugehörigen Anteile und Bahnen: fast vollständige Agenesie der neo-cerebellären Hemisphären mit starker Unterentwicklung des Wurmes und der Flocken. In Zusammenhang mit diesen schweren Missbildungen steht die symmetrische Hypoplasie der Brückenarme, des Brückengraus und der Brachia conjunctiva. Im weiteren imponiert eine starke Entwicklungshemmung des gesamten vestibulären Systems, besonders der lateralen Kernsäule, deren Bedeutung unter Berücksichtigung der Literatur eingehend diskutiert wird. In unserer Beobachtung fand sich eine angeborene diffuse, generalisierte Hyperostose. Der Zusammenhang zwischen den Knochenveränderungen und den Entwicklungshemmung im Zentralnervensystem ist nur indirekt zu verstehen und wird als Effekt einer unbekannten Noxe gedeutet. Da in der gesamten Literatur keine Veröffentlichung eines ähnlichen pathologischen Bildes gefunden werden konnte, rechtfertigt sich die ausführliche Beschreibung und Diskussion des vorliegenden Falles.

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ON SERUM COPPER IN PATIENTS WITH SCHIZOPHRENIA

By

SVEN MUNCH-PETERSEN

In a monograph on serum copper and serum iron *Heilmeyer, Keiderling & Stüwe* (1941) (1) have presented a material of serum copper values from patients with schizophrenia. In 27 patients aged 16 to 44 they generally found enhanced serum copper, one third of the values even exceeding 200 γ %, which is twice the average value stated for normals (106 γ % for both sexes). Only in a few fresh cases they observed values similar to those obtained in normal persons, but otherwise they were unable to demonstrate any relationship between degree of severity of the disease and the serum copper level.

My own investigations on serum copper in patients with schizophrenia, which apart from mental suffering did not show anything abnormal with the exception of a very slight anemia, do not verify the results which Heilmeyer et al. have presented. I have not found any difference between serum copper values in normals and in patients with schizophrenia.

METHODS

For the determination of serum copper the previously mentioned colour reaction with sodium diethyldithiocarbamate was used (3). Duplicate determinations were carried out with a maximum deviation of 10 γ %.

The blood sedimentation rate was determined ad modum *Westergren* (1922) (4).

The hemoglobin percentage was determined by the "sicca" method given by *Hesse & Trier* (1937) (2).

CASE MATERIAL

In the department from which the case material originates there was a very large number of patients with schizophrenia. In the investigations, however, only such patients have been included as did not show any sign of infections, as infections are often known to give rise to an increase of serum copper.

The author has of course been aware that it is a fundamental assumption in using the material that the diagnosis schizophrenia is as sure as possible. The greatest precaution has therefore been exercised in selecting the case material. As, probably, in this country the diagnosis of schizophrenia is drawn with narrower bounds than is the case in practically all other countries it is justifiable to believe that the patients included in the material would have been diagnosed as schizophrenics by any psychiatrist.

The duration of the illness has in no case been less than 2 years, in men varying between 2 and 32 years and in women between 4 and 24 years.

The material hereafter comprises 24 men with schizophrenia, aged 21 to 50, and 16 women with schizophrenia, aged 23 to 48 years. Most of the patients have been treated with shock generally by means of insulin and often combined with metrazol shock, or since 1943 with electroshock. The shock-treatment, which was never given immediately before the drawing of blood, had at most a transient effect. The patients as a rule were quiet when the blood samples were taken and only in a few cases antagonistic.

All the men in the material had a hemoglobin percentage above 90 and all the women above 80. This means that in some of the patients a slight anemia was found. All the men had a blood sedimentation rate below 7 mm, and all the women below 10 mm.

The blood samples were all drawn between 9 a.m. and 10 a.m., the patients having had breakfast at 8 a.m. The examinations were undertaken during the winter 1947 to 1948.

RESULTS

The results are reported in Table 1.

It appears from the table, that the limits for serum copper in 24 male patients with schizophrenia are 76 to 146 γ % (average: 109.50 γ % $\pm$ 4.0, σ = 19.41). In the 16 female patients with schizophrenia

TABLE 1
Patients with Schizophrenia.

Case	No.	Age	Duration in years	Hgb. %	S.R.mm. 1 hour	Serum copper γ %
<i>Men:</i>						
8946/16	1	49	32	99	3	144
11049/26	2	46	23	96	7	146
11814/29	3	39	19	105	5	143
16266/42	4	30	8	93	2	117
14155/37	5	36	15	106	4	94
14298/38	6	33	13	111	4	76
16204/42	7	43	16	105	6	112
18144/46	8	39	11	102	2	105
16843/44	9	35	14	99	4	101
9151/17	10	49	30	109	3	93
11040/26	11	41	22	106	6	101
13841/36	12	43	16	92	3	110
13812/36	13	46	19	98	4	131
18390/46	14	35	10	107	4	136
15881/42	15	35	12	112	4	124
18620/47	16	30	2	103	4	99
18971/47	17	33	10	107	2	106
18190/46	18	40	6	92	2	84
18661/47	19	26	3	102	3	100
19087/48	20	25	9	112	1	95
15993/42	21	32	12	106	2	92
19151/48	22	20	3	98	2	97
16712/43	23	27	4	103	5	122
17259/45	24	42	19	103	2	100
<i>Women:</i>						
17994/46	1	39	4	101	6	120
19019/47	2	25	4	93	8	109
19028/47	3	23	4	86	6	91
15826/41	4	36	11	97	4	89
17129/44	5	34	17	94	6	119
14956/39	6	43	9	94	9	108
17447/45	7	33	11	99	9	98
12137/40	8	40	24	87	6	126
19007/47	9	31	5	92	2	120
17525/45	10	23	4	96	4	115
13441/35	11	46	13	99	4	127
14685/39	12	33	11	98	5	123
19128/48	13	47	10	96	10	139
18529/47	14	32	4	93	6	137
18253/46	15	37	4	94	3	98
19063/48	16	36	13	91	8	119

serum copper varies between 89 and 137 γ % (average: 114.88 γ % $\pm$ 3.8, σ = 15.02). In my normal material (see (3)) consisting of adult normal persons with an age distribution as in the patients, there was found in 50 men the limits 81 to 164 γ % (average: 108.20 γ % $\pm$ 2.1, σ = 15.15) and in 50 women the limits 73 to 152 γ % (average: 118.54 γ % $\pm$ 2.2, σ = 15.65). It thus appears that in patients with schizophrenia the serum copper values lie within the same limits as for normal persons. The average values of the patients are also in good agreement with the averages for normals, even if the mean value for men is a little higher and for women a little lower than the averages in the normal material. The differences are not significant, the t-values being 0.29 for men and 0.84 for women. The average for women with schizophrenia is stated by the author to be higher than for men with schizophrenia, as is also the case in the normal material. In the patients, however, one cannot speak of a significant higher average value in the women, this probably being due to the comparatively small case material.

DISCUSSION

It should be mentioned that in a few patients with schizophrenia enhanced serum copper values were found, but in these patients the blood sedimentation rate was always enhanced, too, which presumably indicates a latent infection.

As mentioned above, Heilmeyer et al. as a rule find enhanced values in patients with schizophrenia. They have also considered whether this increase was of infectious or toxic origin. They think that it is justifiable to exclude the infectious genesis, at any rate in 5 of the 27 patients which they have examined, because the 5 persons have normal values of serum iron and -protein. As no information of infection in their 22 other patients is available, they assume that there is a certain connection between schizophrenia and the enhanced serum copper values. Unfortunately, however, they do not give any report of the blood sedimentation rate in their patients. A satisfactory explanation cannot be offered why Heilmeyer et al. obtained raised values of serum copper and why the present author was unable to reproduce this observation.

CONCLUSION

In a case material of physically healthy men and women with schizophrenia the serum copper values were found within the same limits as in normal persons, which is contrary to the statement by

Heilmeyer et al. that the serum copper is enhanced in this disease. The average values are in good agreement with the averages of my normal material and as in the case of normals, the mean value of the female patients exceeds that of the male patients.

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A CASE OF INTERNUCLEAR OPHTHALMOPLÉGIA (BIELSCHOWSKY) WITH AUTOPSY

By

ERNST SAHLGREN and ERIK HOFMAN-BANG

Woman, age 62 years.

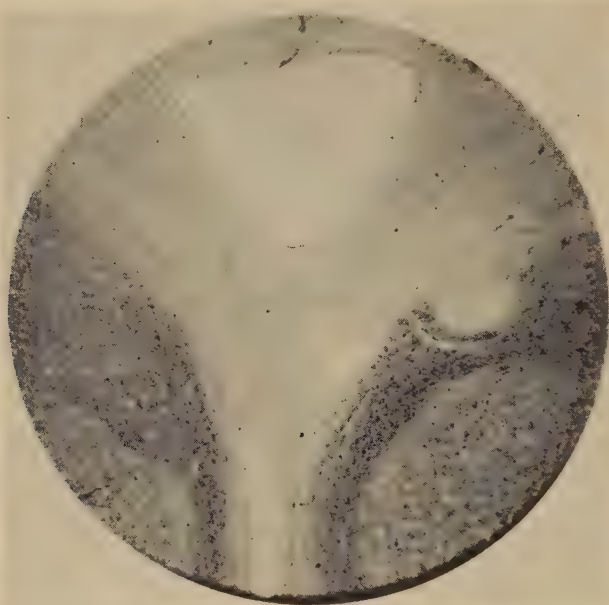
On the whole healthy until 1925, when she began to feel tiredness in her legs. This tiredness increased and she walked with difficulty; besides she suffered from precipitancy of micturition. In 1926 she was treated at the Åsö Hospital, where it was found that the right eye did not accompany the left when looking to the extreme left but returned to the middle position. No nystagmus, the other cranial nerves without comment, except no. XII—deviation of the tongue to the left. Her strength, superficial sensation and sense of position without comment. No atrophy. Romberg? Inversion of the plantar reflex on both sides. Patellar reflexes brisk. No clonus. Gait unsteady. Correct pointing test. Adiadochokinesis? Forfinger-nose and heel-knee tests without comment. Abdominal reflexes absent. Pupillary reflexes and the eye-grounds without comment.

During the following years the symptoms grew worse. For the last few years she had only been able to sit. Weakness in her arms. Could eat, but not work with her hands. Her vision had declined little by little. Incontinentia urinae et alvi. The last days before admission to S:t Eriks Hospital on the 10th of September, 1940, her temperature was about 38° C. On examination of the nervous system the patient was found to be slow; orientation without comment. Remote and recent memory rather good. Speech without comment. Eye-grounds without comment. Pupils medium-sized, equal, and round. When looking aside each eye, alternatively, remained fixed. No diplopia. No nystagmus. Slight paralysis of the lower limb with patellar reflexes and ankle-jerk lacking. Babinski positive on the left. Positive (?) on the right side. Abdominal reflexes lacking. Greatly reduced strength in arms and hands which were somewhat spastic with positive radial jerks. Slight atrophy of the hands. Sense of position without comment. Superficial sensation difficult to test. Incontinence of the bladder. Diadochokinesis very slow bilaterally.

Unfortunately the convergence and pupillary reflexes were not tested. It was not possible to make an oto-neurological examination. Haemoglobin 59 per cent. Red blood cells 3.05 mill.

She died 13/9 1940.

Autopsy showed slight arteriosclerosis of the aorta and very slight coronary arteriosclerosis; slight, old endocarditic adherences of the valvulae aortae. Small embolus in the left pulmonary artery. There was the beginning of a catarrhal pneumonia in the right lung. Pyogenic haemorrhagic cystopyclitis and a little gastric ulcer.



The examination of the central nervous system showed numerous larger and smaller sclerotic lesions which were disseminated from the frontal region down to the 5th lumbar segment. Consecutive sections through the midbrain and pons showed a well confined lesion the size of a pinhead directly under the lateral part of the oculomotor nucleus in the right dorsal longitudinal fasciculus (see fig.). Motor nerve cells, single and intact, were found scattered in this lesion. The more caudal sections disclosed an increasing deterioration of the right dorsal longitudinal fasciculus, which in its whole length was destroyed on a level with the outlet and the decussation of the troclear nerve in the anterior medullary velum. Both the dorsal longitudinal fasciculi were intact between the troclear decussation and the troclear nucleus. They were also intact on a level with the abducens nucleus whose cells did not show any changes.

The symptom in question has been described by several authors: von Bielschowsky 1902, Uthoff and others.

Antoni in 1917 (published 1919) described three cases of bilateral paresis of the internal rectus muscles together with nystagmus when looking aside, all cases of disseminated sclerosis. Convergence ability was preserved. He had no post-mortem to prove his point, but accepted

as an explanation an interruption on both sides of the fasciculus longitudinalis posterior between the nuclei n. abducentis et oculomotorii.

Bielschowsky had given the same explanation. The voluntary impulses for the side glance reach abducens, but not the nucleus of rectus internus. This explains the symptom that the one eye is left behind when looking aside.

In the case described by Antoni the vestibular excitability of the rectus internus was reduced, that of the rectus externus preserved. This agrees with the assumption that the vestibular impulse *follows* the voluntary impulse. Antoni had no autopsied case then, but later, according to a statement made in a lecture not yet printed, he had received one. Besides this case, it seems that only Spiller has published a case studied post-mortem.

Clinically it was found that the disappearance of rectus internus function was bilateral with the side glance, but intact function through convergence. Besides, slight paresis of the left obliquus superior.

Softening in the left and, but less noticeable, in the ventral part of the right fasciculus longitudinalis was observed from the section. Besides there was a destruction of the left trochlear nucleus, especially in the upper section. (It may be presumed clinically, that a mistake has been made as to side of the trochlear paresis).

Our case had not been thoroughly examined. A vestibular test could not be made because of the patient's condition. Through unfortunate circumstances, the convergence ability was not examined during the last hospitalisation. During hospitalisation in Åsö Hospital it can be assumed that the convergence was tested and found to be normal. The case is important because of the slight radius of the lesions. The one at the right fasciculus longitudinalis posterior explains the reduced ability to direct the left eye to the right; the other lesion which was under the right oculomotor nucleus, explains the lack of ability of the right rectus medialis to turn the eye to the left, as it may be presumed that the passage from the left oculomotor nucleus passes through there to the right m. rectus medialis. Our case, therefore, in spite of incomplete examination, supports the theory of Bielschowsky, Antoni, and others, on the localisation of the injury when the symptoms are those mentioned above.

UN NOUVEL APPAREIL DE PNEUMOENCEPHALOGRAPHIE

Par

BASILE YAGDJOGLOU

Plusieurs instruments de pneumoencéphalographie, tels ceux de Bingels, Benedick, Schintz, Wertenberg, Liberson, Stroch, Osborne, portant le nom de leurs créateurs ont été inventés jusqu'à aujourd'hui. Parmi ces appareils, il en est certains dont l'emploi est facile et pratique tout comme il en est d'autres dont l'usage est difficile et compliqué. Nous employons, dans la clinique de Psychiatrie de Bakirköy, une aiguille pour ponction lombaire spéciale, d'usage simple et de fabrication facile et peu coûteuse.

Sa particularité réside dans le fait qu'elle rend possible l'association simultanée d'une donnée d'air, d'une évacuation de liquide cérébro-spinal et d'un contrôle permanent de la pression.

Le principe de l'appareil comprend deux aiguilles qui se pénètrent concentriquement. La première aiguille (A fig. I) est une aiguille ordinaire pour ponction lombaire, ayant 10 cm. de long sur 2 mm. de diamètre.

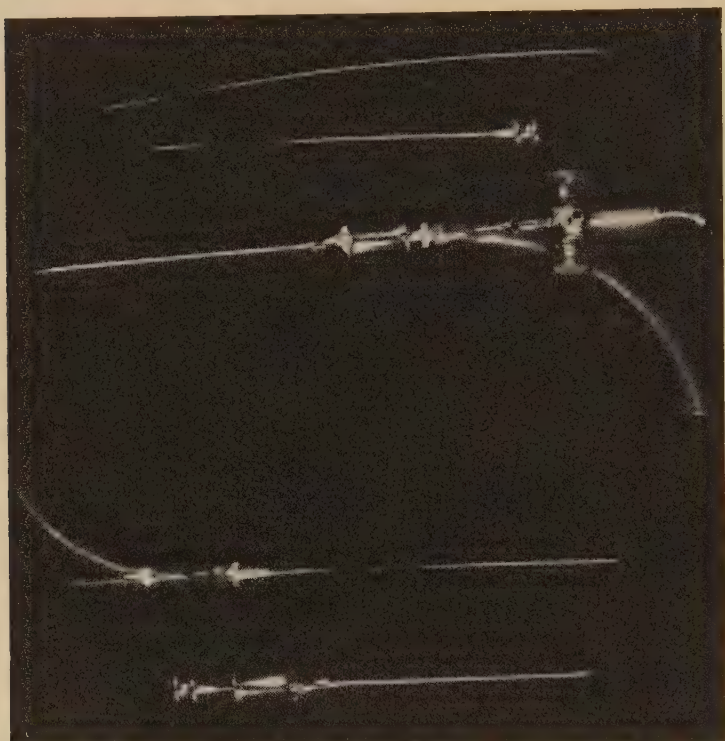
La deuxième aiguille (B fig. II) qui pénètre à l'intérieur de la précédente est une aiguille de 15 cm. de long sur 1 mm. de diamètre, de celles que l'on emploie communément pour les anesthésies par infiltration.

Un bec s'adaptant étroitement à l'aiguille pour ponction lombaire constitue la troisième partie de l'appareil.

Avant d'opérer la ponction nous fixons la partie postérieure du bec à celle d'un tube en caoutchouc de 40 cm. de longueur auquel nous ajoutons l'aiguille (B) en lui faisant percer le tube et traverser le bec. (Fig. III). Après avoir stérilisé l'instrument ainsi obtenu nous opérons la ponction avec l'aiguille A. Dès que les premières gouttes de liquide commencent à paraître, nous enfonçons l'aiguille (B) et le bec à l'intérieur de l'aiguille (A) à l'instar d'un mandrène, de

façon que le bout de l'aiguille B dépasse de 4—5 mm celui de la ponction lombaire. (Fig. IV).

Le bec une fois étroitement adapté à la racine de l'aiguille pour



ponction lombaire (A) nous retirons le mandrène de l'aiguille B et le liquide commence à couler.

Après avoir prélevé de l'air sur une flamme à l'aide d'un injecteur stérile, nous adaptons ce dernier à l'extrémité libre en caoutchouc et commençons la p. e. g.

Nous ouvrons le robinet pour entraîner l'évacuation du liquide sur la pression duquel nous renseigne un manomètre de Claude adapté à l'aiguille B.

Après avoir prélevé I cc. de liquide nous injectons 0,8 cm³ d'air.

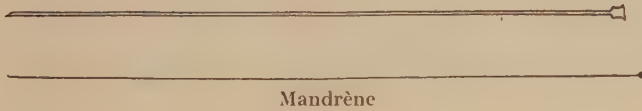
Le liquide ainsi évacué est ramassé dans une éprouvette graduée qui nous fixe sur la quantité d'air à injecter. Nous en injectons généralement 20 cm³ pour un équivalent de 25 cm³ de liquide ; 60 à 70 cm³ d'air suffisent pour encéphalographie complète.

Injecté parallèlement à l'évacuation du liquide cérébrospinal, l'air



Mandrène

Fig. 1.
Aiguille A



Mandrène

Fig. 2.
Aiguille B

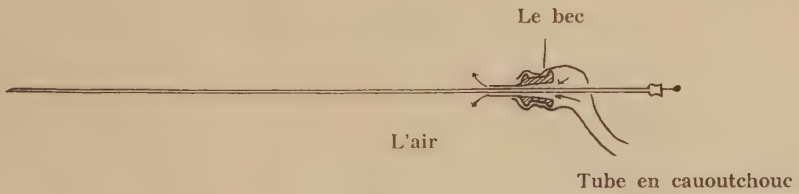


Fig. 3.

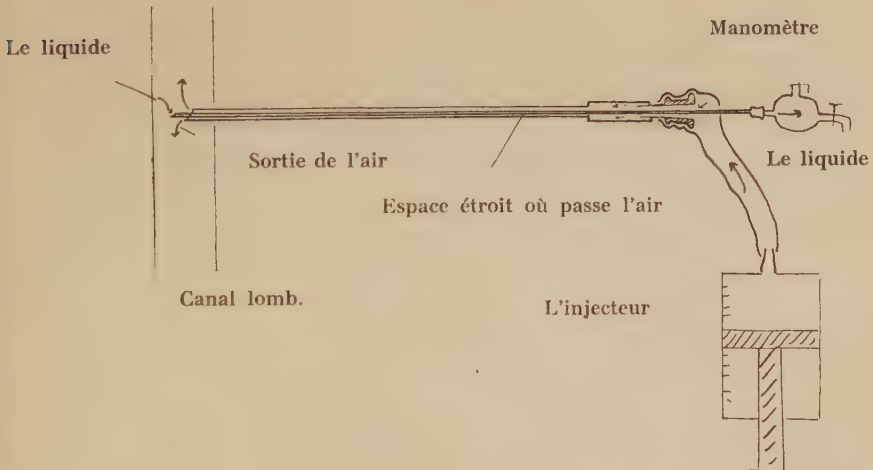


Fig. 4.

arrive à destination par l'extrémité de l'aiguille pour ponction lombaire, après avoir traversé l'espace étroit compris entre les deux aiguilles.

Il est bon de fermer le robinet par intervalles afin de contrôler la pression, comme il est nécessaire aussi de faire attention au maintien

de celle-ci au niveau initial afin d'éviter des symptômes bulbaires désagréables tels que transpiration, pâleur, vertiges, maux de tête, vomissements etc.

L'air ainsi fourni par doses progressives entraîne une grande diminution des symptômes précités.

La facilité pratique de la méthode ainsi que la simplicité et le coût insignifiant de l'appareil nous ont donné le courage d'en faire la publication.

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THE ISOLATION FROM THE BLOOD OF CHRONIC SCHIZOPHRENIC PATIENTS OF COMPOUNDS ACTIVE IN RADIOACTIVE PHOSPHATE TURNOVER

By

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Biochemical Nobel Institute and Långbro Mental Hospital.

This work is an attempt to isolate and purify from blood corpuscles the phosphorus compounds most rapidly labelled with radioactivity after the injection of radiophosphate in cases of chronic schizophrenia.

The background of this attempt is as follows:

We started several years ago with studies on the possibility of detecting disturbances in metabolism in chronic schizophrenic cases with special reference to the phosphate esters. These esters are important from several points of view, viz. as energy transmitters in intermediate metabolism. These studies did not give as many positive results as expected. The use of radioactive substances opened new approaches to the problem. This method gave results which will be briefly described in what follows.

We add the radiophosphate in the form of free radioactive orthophosphate intravenously. The quantity of phosphate added is only some few milligrams. The radioactivity amounts to between 800,000 to 8 million impulses per minute (0.01 to 0.1 milliCurie).

The relation between the radioactivity expressed as impulses per minute and phosphate in γ in the different phosphate fractions is called the specific activity (Spec. act. = P_{32}/P). The higher this value the more rapid the turnover (Borell and Örström).

Table 1 is a comparison between the spec. act. in chronic schizophrenic cases and normal persons in some phosphate ester fractions.

The spec. act. of *ATP* shows a marked decrease 15 min. after injection of P_{32} in chronic schizophrenic cases from 0.26 in the

TABLE 1

The specific activity in some phosphate fractions in chronic schizophrenia.

Time after inj. of	Controls (n=19-20)		Chr. Schiz (n=28)	
	15 min.	24 hrs.	15 min.	24 hrs.
0.01 mC P32	15 min.	24 hrs.	15 min.	24 hrs.
Spec. act. free P	1.84 $\pm$ 0.084	0.32 $\pm$ 0.044	2.24 $\pm$ 0.150	0.35 $\pm$ 0.026
" " ATP (Adeno- sintriphos- phoric acid)	0.26 $\pm$ 0.058	0.029 $\pm$ 0.009	0.041 $\pm$ 0.009	0.026 $\pm$ 0.006
" " residual fraction	0.026 $\pm$ 0.007	0.087 $\pm$ 0.008	0.015 $\pm$ 0.006	0.110 $\pm$ 0.007
" " tot. org. P	0.050 $\pm$ 0.009	0.079 $\pm$ 0.007	0.016 $\pm$ 0.003	0.098 $\pm$ 0.006

control cases to 0.04. This value is supported by differences found in the spec. act. of the total organic phosphate.

It must, however, be emphasized that the differences found here in the spec. act. of ATP are mean values for the group concerned. The individual values show great variation and the method cannot be used in diagnosis. In the control group one finds 15 % of the values for the spec. act. of ATP at zero. The corresponding value for the chronic schizophrenic group is 48 %. The highest value in the control group is much higher than the highest value in the schizophrenic group.

We add P32 in the form of inorganic orthophosphate. This labelled phosphate is very rapidly transferred into organic compounds. The substance which directly combines with the inorganic orthophosphate must have a very strong correlation to it. In order to decide if there was a difference between chronic schizophrenic cases and control cases in the correlation between the spec. act. of the free phosphate and the spec. act. of different phosphate fractions the coefficient of correlation (r) was calculated in a larger series. The concentration of radioactive phosphate ranged between 0.01 to 0.1 milliCurie.

The following values were obtained.

TABLE 2

The coefficients of correlation between spec. act. of orthophosphate and different phosphate fractions in chronic schizophrenia.

Correlation between spec. act. of	Control cases and Chr. Schiz.			
	15 min. n=31	24 hrs. 29	15 min. 71	24 hrs. 55
P and tot. org. P	0.901	0.635	0.637	0.760
P and ATP	0.634	0.422	0.217	-0.299
P and residual fraction	0.659	0.723	0.722	0.800

In Table 2 it is shown that the spec. act. of ATP has a good correlation to the spec. act. of free P 15 min. and 24 hrs. after the injection of P32 in the control cases. The chronic schizophrenics, however, show no correlation between the spec. act. of these both fractions, neither after 15 minutes nor 24 hours. In the spec. act. of the *total org. P* and the residual fraction there is a good correlation to spec. act. of free P both in control cases and schizophrenic cases.

In chronic schizophrenic cases there are thus other phosphate compounds than ATP having a correlation to the free phosphate.

It might be supposed that this unknown phosphate ester might play a role in the metabolism of schizophrenia and so we tried to isolate and purify the phosphate ester fractions which in chronic schizophrenia are most rapidly labelled with radioactivity and have a correlation to the spec. act. of free phosphate.

These purifications have continued for the last two years and we have together made 19 preparations. Each preparation in general consists of 4 litres of blood corpuscles from normal healthy persons and 0.5 litre whole blood from chronic schizophrenic patients having been injected with 0.2 mC P32 to label the substance.

We have during these preparations used about 150 litres human blood, and 15 litres from schizophrenic patients. Such large quantities of blood must be used because the unknown so-called schizophrenic esters are found only in a concentration of 0.5 mg%. They are found only in the blood corpuscles in healthy persons as well as in schizophrenic patients. They have not been found in blood from horses or oxen.

We soon in blood from schizophrenic patients found two phosphate fractions, each of them being more active than ATP normally. One was precipitated at pH 1.5-3 as mercury-salt. It was called *Hg-x*. The other was precipitated by pH 8 as Ca-salt from 80 % methanol. It is called *rest-x*. *Hg-x* has always a higher spec. act. than *rest-x*.

Very soon we suspected that *Hg-x* was not an organic phosphorus compound but an inorganic substance. It formed salts with Fe Ba Al which all precipitated at pH 1.5-3, lower than the limit for the known organic phosphate esters. We then had to chose between pyrophosphate and metaphosphate. Pyrophosphate could be excluded because it forms an insoluble cadmium salt (Cohn and Kolthoff), which *Hg-x* does not. The purest preparations we have precipitated as Ba-salt show hydrolysis curves and precipitation similarly to metaphosphate. An analysis of this preparation showed that it contained about 20 % adenylic acid. A determination of C and H showed a value corresponding to the adenylic acid content. The rest is inorganic.

It contained about 20 % P. All these facts taken together strongly indicate that Hg-x is metaphosphate. It is not clear whether it is free or combined with adenylic acid. One of the impurities which are most difficult to eliminate is adenylic acid.

The metaphosphoric acid precipitates proteins contrary to the other phosphoric acids which do not. The pure prep. of our compounds also precipitates proteins.

Metaphosphate has also been found in yeast and in mycelium from aspergillus (Max Farlane, 36, Mann, 44). Some indications are also found for its presence in brain and muscle from animals (Mann, 44).

In yeast two kinds of metaphosphate are found. One fraction is free and has a very slow turnover, the other fraction is bound to proteins and has the highest turnover of all phosphate esters if the turnover is measured with P32 (Kalckar et al., 48).

The other compound we have been trying to isolate is *rest-x*. It is easily soluble but difficult to hydrolyse. Its chemical composition is unknown, but we have preparations up to 20 % P. But we have not enough for analysis.

At the same time as these purification experiments we carried out analyses of the spec. act. of Hg-x and *rest-x* in smaller samples of blood—40 ml—to get an approximative estimate of the correlation between the spec. act. of these two fractions and the spec. act. of free P. These analyses were carried out with impure preparations and are given with reservation.

Both in normal cases and chronic schizophrenic cases one finds a correlation between the spec. act. of Hg-x and the spec. act. free P.

Contrary to the spec. act. of ATP the spec. act. of Hg-x thus has a correlation to the spec. act. of free P in chronic schizophrenic cases.

For the spec. act. *rest-x* no correlation is found. It must be emphasized that these values may change when the pure substances are available for testing.

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Our acknowledgements are due to Professor Theorell for his profound interest and good advice.

SUMMARY

(1) The radioactive phosphate turnover of different phosphate compounds in blood has been measured in chronic schizophrenic patients. Of all phosphate fractions analysed only the turnover of

adenosintriphosphoric acid, ATP, showed a considerably lower value than the controls (0.04 as against 0.26).

(2) Of all phosphate fractions investigated only the spec. act. of ATP in chronic schizophrenic patients had no correlation to the spec. act. of free P. These two facts together indicate that other phosphate compounds than ATP play a role for the turnover in chronic schizophrenic patients. In control cases there are good correlations in all fractions.

(3) Attempts have been made to isolate the phosphate compounds playing a role in chronic schizophrenia by labelling them with radioactive phosphate. Two different compounds have been isolated. One is so far unknown, the other is metaphosphate, either free or combined with an organic substance.

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Dedicated to W. JASON MIXTER
most respectfully by the authors.

LE PROLAPSUS DISCAL LOMBAIRE

Par

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INTRODUCTION — MATÉRIEL D'OBSERVATION

Par EDUARD BUSCH

Les travaux dont il est rendu compte ci-après sont basés sur l'étude d'un matériel d'observation constitué par des malades souffrant d'un prolapsus discal lombaire, diagnostic vérifié par le Service de Neurochirurgie de l'Hôpital Universitaire de Copenhague. Ils ont été pratiqués dans le but d'étudier plus à fond cette question qui prend une place de plus en plus importante, ceci afin d'arriver à une meilleure compréhension des symptômes de la maladie et de son diagnostic, de la thérapie appliquée et de ses résultats.

En ce qui concerne l'historique du problème de la lombo-sciatique, on est prié de se reporter à des monographies plus importantes (*Bradford & Spurling, Malmros, Norlén*). Nous nous bornerons ici à donner un tableau sommaire (fig. 1) reprenant les désignations appliquées à travers les âges qui reflètent parfaitement la variabilité des conceptions. Différents auteurs se sont attachés, d'ailleurs avec assez d'étroitesse, à une étiologie arthritique, musculaire ou neurogène. Certains cependant ont vu que les causes pouvaient être variées et qu'il pouvait y avoir concomitance de facteurs chez le même malade. Le prolapsus du disque lombaire à l'origine de la lombo-sciatique est venu se placer au premier plan après le travail de *Mixter & Barr*, en 1934. Depuis,

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Fig. 1.
Historique.

1658	<i>Riolan</i>	ischias notha — ischias vera.
1764	<i>Cotugo</i>	ischias nervosa — ischias arthritica.
1841	<i>Valleix</i>	neuralgie sciatique.
1864	<i>Lasègue</i>	neuralgie sciatique — neuritis sciatique. Parfois « plus musculaire que sciatique ».
1876	<i>Helleday</i>	myitis chronica.
1908	<i>Petrén</i>	affection musculaire primaire ?
1914	<i>Forestier</i>	pathogénie sacrovertébrale.
1916	<i>Léri & Schaeffer</i>	origine radiculaire, rôle des canaux sacrés.
1918	<i>Sicard</i>	sciatique funiculaire, arthrite vertébrale.
1920	<i>Helweg</i>	myopathia e labore.
1920	<i>Lindstedt</i>	réflexe neuralgique par suite de myopathie.
1925	<i>Danforth & Wilson</i>	arthrite lombosacrée influençant L5.
1928	<i>Feiling</i>	neurite interstitielle, périneurite dans L5.
1929	<i>Grossmann & Keschner</i>	sciatique neuralgique ostéoarthritique.
1934	<i>Mixter & Barr</i>	rupture du disque intervertébral.

leur observation a été confirmée par l'évolution dans la plupart des pays, bien qu'on ait eu tendance parfois soit à la bagatelliser, soit à en surestimer la valeur. Peu à peu, le tableau de la maladie et sa thérapie semblent néanmoins se préciser.

Définition.

Un prolapsus discal intrarachidien est un prolapsus de tissu du nucléus pulposus qui, à la suite d'une rupture de l'annulus fibrosus pénètre dans le canal rachidien ce qui, par pression exercée sur les racines nerveuses, peut provoquer à la fois une irritation avec douleurs et spasmes et une paralysie avec les répercussions qu'elle entraîne. En radiologie, on a souvent utilisé l'expression « *îlots cartilagineux de Schmorl* », en pensant au prolapsus du tissu pulposus dans les corps vertébraux adjacents. Ces îlots de Schmorl n'ont rien à voir avec les prolapsus intrarachidiens et il est peu fréquent qu'on les rencontre simultanément avec ceux-ci.

Pathogénèse.

Deux origines paraissent vraisemblables : soit un trauma, souvent un gros effort ayant provoqué une rupture de l'annulus fibrosus suivi immédiatement ou plus tard d'un déversement de tissu pulposus dans le canal rachidien, soit une dégénération primaire du tissu pulposus rendant le disque instable, la mobilité entre les vertèbres devenant plus grande et moins souple que de normale. A la suite des nombreux



Fig. 2.
Prolapsus paramédian comprimant
une racine.



Fig. 3.
Prolapsus paramédian comprimant
deux racines.

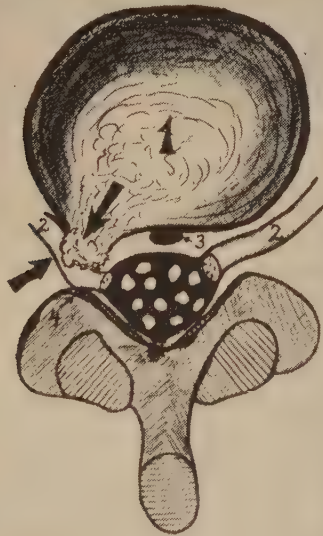


Fig. 4.
Prolapsus latéral.

traumas de la vie courante, l'annulus tendu et courbé de façon anormale finit par se rompre et le prolapsus se produit. Nous ne savons pas encore laquelle de ces causes est la plus fréquente, mais nous avons dans notre matériel d'observation des cas qui illustrent clairement les deux possibilités. Il est évident que le trauma a son importance dans les deux éventualités. Nous montrerons plus loin qu'il est possible de le retrouver dans l'anamnèse d'un grand nombre de cas, les malades s'en souvenant même au bout de plusieurs années. La répartition par catégories professionnelles des malades souffrant de prolapsus semble d'ailleurs indiquer la même chose. A l'heure actuelle, nous ne pouvons toutefois pas établir avec certitude si dans la plupart des cas le trauma est la cause directe de la maladie ou s'il joue le rôle de déclencheur, bien que l'on arrive généralement à l'établir dans les cas particuliers.

Les différentes formes de prolapsus.

A l'opération, le prolapsus du disque se présente le plus souvent comme une masse compacte de tissu pulposus blanchâtre, filandreux. La rupture de l'annulus peut généralement être observée directement et nous distinguons, suivant sa localisation, entre les prolapsus *paramédians* et *latéraux*. Les prolapsus *paramédians* sont les plus fréquents (plus de 80 % de nos cas) ; ils peuvent provoquer aussi bien des symptômes unilatéraux que bilatéraux — ces derniers toutefois souvent après plusieurs années de maladie, au fur et à mesure que grossit le prolapsus sous la pression vers l'extérieur d'une masse toujours croissante de tissu pulposus. Le prolapsus *latéral* est ordinairement plus petit que le paramédian, mais provoque toutefois rapidement des symptômes, étant situé dans le trou intervertébral ; il est toujours unilatéral. Au cours de ces dernières années, nos connaissances se sont étendues sur ce que nous appelons le *prolapsus incomplet* où l'on a constaté à l'opération que l'annulus, au lieu d'être dur et résistant comme à l'état normal, était bien entier, mais aminci comme une feuille de papier et fortement renflé. Si cette couche extérieure très mince est déchirée, on constate qu'il existe à l'intérieur un prolapsus tout prêt, facile à déplacer. Le prolapsus incomplet peut provoquer des symptômes uni et bilatéraux. On peut observer de plus ce que nous appelons le « *disque relâché* » dans lequel l'interligne entre les deux vertèbres adjacentes au disque atteint peut être diminué d'un centimètre en appuyant sur les apophyses épineuses, ceci ne pouvant ordinairement se produire que pendant la narcose au cours de laquelle se relâche la fixation musculaire. Dans le prolapsus in-

complet, il est question d'une véritable hernie du nucléus pulposus, mais nous l'appelons *prolapsus incomplet* pour des raisons de terminologie pratique. Les américains le désignent le plus souvent comme un « *protruding disc* », ce qui ne dit rien du nucléus séquestré dans l'annulus qui fait saillie.

Le prolapsus peut parfois être *total*. Nous entendons par là que la masse entière du nucléus s'est déversée et que l'intérieur du disque est vidé de son tissu pulposus; ces gros prolapsus libres peuvent parfois « circuler » dans le canal rachidien pour trouver de la place, passant même entièrement sur la face dorsale de la dure-mère. La plupart des formes de prolapsus peuvent être rattachées à une *rupture du ligament longitudinal postérieur* et il semble que les symptômes bilatéraux soient particulièrement fréquents.

Douleur causée par le prolapsus et son origine.

De quelle manière les symptômes résultant d'un prolapsus intrarachidien se manifestent-ils ? Dans certains cas par les compressions du sac dural et de la queue de cheval contre les parois du canal rachidien, de sorte qu'il se produit une paraparésie flasque avec bloc rachidien total ou partiel, exactement comme dans les tumeurs de la queue de cheval (fig. 5). Ce cours de maladie est cependant rare et on l'observe notamment lorsqu'il y a un gros prolapsus total aigu. Dans le plus grand nombre des cas, une seule racine est comprimée dans le trou intervertébral qui est limité antérieurement par le disque, postérieurement par le bord tranchant du ligament jaune.

La pression exercée sur la racine provoque les douleurs « radiculaires » typiques, la *douleur sciatique* irradiante caractéristique, accentuée sous la pression abdominale, irradiant sur le côté postérieur de la cuisse, sur le côté postérieur ou extérieur de la jambe ou dans les orteils, suivant la racine qui est comprimée. Nous devons considérer maintenant comme certain que la compression radiculaire est réellement la cause de la douleur sciatique chez les malades du prolapsus : quand nous opérons un malade avec anesthésie locale, nous pouvons à notre gré, aussi souvent que nous le désirons, provoquer les douleurs typiques à ce malade par irritation de la racine incarcérée et seulement par irritation de celle-ci. Au contraire, la douleur peut être supprimée par le blocage à la novocaïne de cette racine.

La plupart de nos malades souffraient en plus de la sciatique de *douleurs lombaires* qui étaient souvent plus anciennes dans l'anamnèse que leur sciatique. Le lumbago s'explique vraisemblablement par une rupture complète ou partielle de l'annulus — la partie posté-

rière de l'annulus étant innervée par une branche récurrente du nerf rachidien correspondant — et c'est souvent ce premier trauma qui est très violent, si violent que les malades se souviennent bien des années plus tard de ce « tour de reins », bien qu'il n'ait généralement été suivi que d'un lumbago et non d'une sciatique : au bout de quelques semaines, les symptômes disparaissent (la compression radiculaire *peut cependant se produire immédiatement*), mais au cours

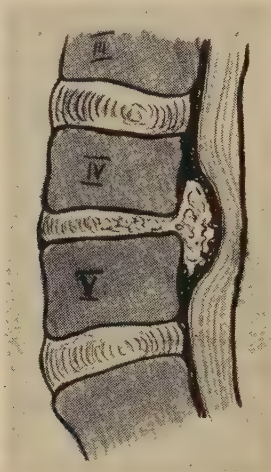


Fig. 5.

Gros prolapsus paramédian comprimant la queue de cheval.

des mois ou des années qui suivent, la masse du tissu pulposus prolabé augmente constamment sous la pression discale croissante due à la charge normale de la position verticale, aux mouvements de la colonne ou aux petits traumas — ce que nous appelons les *traumas secondaires* ou *occasionnels* qui provoquent souvent chez ces malades, dans les premières années, de nouveaux lumbagos. C'est seulement quand le prolapsus est devenu si gros que la racine comprimée donne lieu à la première attaque de sciatique qui, d'ailleurs, disparaît généralement d'elle-même au repos ou après traitement physiurgique approprié — soit parce que le prolapsus change de position par rapport à la racine — (nous pensons ici à l'effet d'un traitement par extension ou d'un traitement de chiropraticien), soit parce que le volume et la teneur en eau du prolapsus se modifient. Enfin, il ne faut pas oublier que le trou intervertébral rétréci par le prolapsus n'est qu'un des facteurs

de la compression radiculaire l'autre étant la racine elle-même. En opérant des cas au cours de la crise, nous avons souvent trouvé la racine incarceration fortement enflée et oedémateuse avec des vaisseaux très encombrés (le déversement des veine a lieu le long de la racine rachidienne), mais ces modifications peuvent évidemment disparaître spontanément.

Dans de rares cas l'incarcération de la racine se produit immédiatement, le plus souvent après un violent trauma. Il se forme de suite un prolapsus total et les symptômes ne diminuent pas. Il y a dès le début parésies, des troubles sphinctériens avec rétention ou incontinence. C'est le groupe que *Malmros* appelle *prolapsus au cours continu*. Le malade est ordinairement hospitalisé au bout de quelques semaines et l'opération est évidemment aussi rapidement indiquée ici que dans les cas de tumeur rachidienne.

Depuis les travaux de *Mixter & Barr*, on a essayé cliniquement de poser le diagnostic de la racine qui, chez un malade donné, est incarceration, ce qui théoriquement paraît possible, aussi bien en se basant sur la localisation de la douleur radiculaire que sur les symptômes neurologiques d'abolition. Au cours des premières années, on n'a toutefois réussi que pour le prolapsus du 3^{ème} disque lombaire, aussi bien les américains que *Malmros* ayant démontré que le prolapsus qui comprime L4 provoque des douleurs sur la partie antérieure de la cuisse. C'est seulement après les recherches de *Norlén* (1944) que nous avons une base plus ferme pour établir le diagnostic clinique du niveau, ses minutieuses études sur le cours des douleurs radiculaires montrant qu'une douleur irradiante dans le talon correspond dans la plupart des cas à la répartition des dermatomes de *Keegan* et indique une compression de S1 — par conséquent un prolapsus du 5^{ème} disque. En effet, par suite du cours oblique de la racine, le prolapsus comprime généralement la racine se trouvant au-dessous du disque. Dans ces prolapsus, on constate aussi souvent une *aréflexie du tendon achilléen*. Une douleur irradiant dans le gros orteil indique souvent la compression de L5, donc un prolapsus du 4^{ème} disque, le réflexe achilléen étant généralement intact. L'analyse de nos observations a confirmé dans l'ensemble les résultats de *Norlén*. Il faut d'ailleurs se contenter d'une concordance très approximative avec les faits anatomiques, étant donné que la position du prolapsus peut varier chez les différents malades et que la compression peut s'exercer non seulement sur la racine située au-dessous du prolapsus, mais sur d'autres et que, d'autre part, les faits peuvent être totalement modifiés par les « déplacements » susmentionnés du prolapsus. Mais il nous est possible maintenant de poser un diagnostic clinique sûr du niveau du prolapsus et nous avons pu

renoncer ces dernières années aux examens pratiqués au moyen des contrastants, si désagréables pour les malades. En plus de l'aide clinique qu'elles nous ont apportée, les recherches de Norlén ont fourni la preuve que chez beaucoup de malades souffrant de prolapsus discal, la douleur sciatique n'est pas seulement de *type radiculaire*, mais qu'elle est réellement *radiculaire*.

On sait d'ailleurs fort bien que l'incarcération de la racine rachidienne n'est pas seulement de *type radiculaire*, mais réellement de nature *radineurogène*, provoquant des *modifications douloureuses de la musculature*. On peut souvent l'observer au cours des opérations où une irritation suffisamment faible peut déclencher des spasmes localisés, des contractions fortes et violentes dans un ou plusieurs muscles. Il paraît très vraisemblable qu'une irritation de longue durée produite par compression de la racine puisse provoquer des modifications dans la musculature innervée par la racine en question. En ce qui concerne les longs muscles dorsaux, ces modifications apparaissent dans les cas débutants sous forme de fixation musculaire due purement à la douleur — une sorte de *défense musculaire* — qui disparaît pendant la narcose et dès que la racine a retrouvé le calme à la suite de l'intervention chirurgicale. Chez les malades souffrant de prolapsus ayant une longue anamnèse, ces modifications peuvent sans aucun doute revêtir un caractère chronique.

Observations.

Les relevés repris par la présente étude ayant été élaborés à des époques différentes, le nombre des malades n'est pas identique dans toutes les parties de ce travail. Une série de nos recherches ont porté sur nos premiers 400 malades. Lorsqu'au contrôle, on n'a pas constaté de modifications importantes chez les malades suivants, les travaux sont rapportés tels qu'ils ont été exécutés. Lorsqu'il a semblé utile, d'un point de vue statistique, d'avoir des chiffres aussi élevés que possible, on a tablé sur le plus grand nombre possible de malades.

Sexe et âge des malades. Sur nos premiers 1000 malades, 537 étaient des hommes et 463 femmes. L'âge des malades au moment de l'opération (fig. 6) montre que plus de la moitié des malades ont été opérés entre 30 et 45 ans, 1/10 seulement ayant dépassé 50 ans. Etant donné que nous avons été très sévères dans l'indication de l'opération, nos malades ont généralement une très longue anamnèse et il apparaît (fig. 7 et 8) que plus de la moitié des malades ont ressenti les premiers symptômes avant leur trentième année — surtout pour ce qui est des hommes, tandis que chez les femmes l'apparition des premiers symptômes est plus également répartie.

Fig. 6.

Age des malades au moment de l'opération (op.) et à l'époque de l'apparition des premiers symptômes (I).

Age			Hommes		Femmes	
	Op.	I.	Op.	I.	Op.	I.
0—10	0	0	0	0	0	0
11—15	1	24	0	9	1	15
16—20	16	127	8	59	8	68
21—25	93	196	49	109	44	87
26—30	110	203	62	108	48	95
31—35	171	165	79	86	92	79
36—40	211	149	98	76	113	73
41—45	193	67	101	46	92	21
46—50	98	37	66	23	32	14
51—55	66	21	52	15	14	6
56—60	27	5	15	4	12	1
61—65	10	3	4	0	6	3
66—70	4	3	3	2	1	1
	1000	1000	537	537	463	463

Localisation des prolapsus. Il ressort de la fig. 9 que tandis que le prolapsus discal peut se produire en n'importe quel endroit du canal rachidien, la plupart des cas opérés sont localisés dans la colonne lombaire et la plupart de ceux-ci sur le 4^{ème} et le 5^{ème} disque lombaire. La colonne dorsale, bien que plus longue, est moins mobile et elle est le plus faiblement représentée, tandis qu'il y a une légère augmentation pour les cas de la colonne cervicale. Les prolapsus cervicaux dépassent le cadre de ce travail; ils ont été décrits au Danemark par *Broager* (1944). Il est frappant de relever que les prolapsus les plus fréquents ou en tout cas ceux qui provoquent le plus fréquemment des symptômes, affectent le 4^{ème} ou le 5^{ème} disque lombaire. C'est sûrement parce que ce sont justement ces disques qui sont les plus exposés, en cas d'effort ou de surcharge. Il est possible aussi qu'il faille en chercher l'explication dans le rapport entre la dimension du trou intervertébral et la racine rachidienne correspondante qui diminue distalement (fig. 10), la racine devenant plus grande, le diamètre du trou plus petit. Que les prolapsus discaux soient dus essentiellement à une dégénération du nucléus pulposus ou qu'ils soient conditionnés par un trauma primaire, il n'y a rien d'extraordinaire à ce que l'on trouve des prolapsus multiples — comme ce fut le cas dans 4,7% de nos observations. Parmi nos 400 premiers disques, 2 malades souffraient de prolapsus multiples, parmi les derniers 600 — pas moins de 45. Il est possible que dans les premières années, nous n'ayons pas

Age at operation.

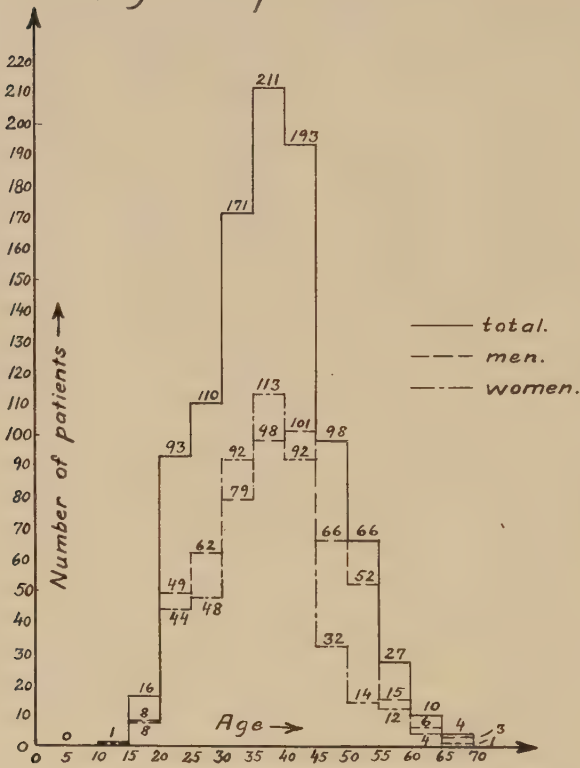


Fig. 7.

Age au moment de l'opération
 Nombre de malades
 ————— total
 - - - - - hommes
 femmes

été aussi attentifs à ce fait et c'est seulement lorsque les malades ont été hospitalisés à nouveau pour ce que l'on croyait être une récurrence que nous avons constaté qu'il s'agissait d'un autre prolapsus, le plus souvent localisé dans le disque sous-jacent. Dans ces cas aussi nous avons observé que c'étaient les deux disques lombaires inférieurs les plus fréquemment atteints.

PROLAPSUS DISCAL ET PROFESSION

Par BENDT BROAGER

Pour étudier l'importance que présente la profession chez les malades souffrant de prolapsus, nous avons divisé nos premiers 400

Age at first symptom.

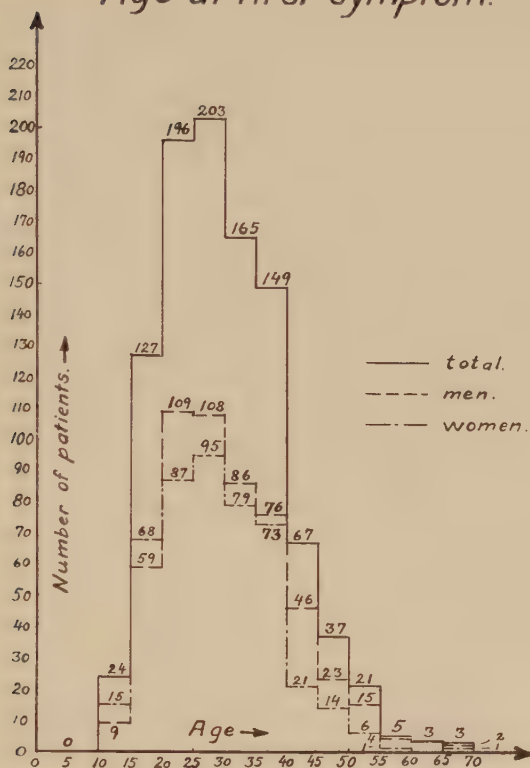


Fig. 8.

Age au moment de l'apparition des premiers symptômes.

Nombre de malades

— total

--- hommes

- - - femmes

malades en 3 groupes d'après les conditions physique requises par leur travail :

Dur travail physique : comprenant agriculteurs, pêcheurs, charpentiers, puisatiers, porteurs d'hôpital et manoeuvres de différentes catégories. Pour les femmes : infirmières, ouvrières de fabriques, femmes de ménage, ménagères de condition modeste ayant une nombreuse famille, etc.

Travail physique moyen : individus qui peuvent avoir à fournir un effort, mais dont le travail est beaucoup moins dur que celui du premier groupe.

Fig. 9.

Service de Neurochirurgie
de l'Hôpital de l'Université 1948.
Prolapsus discal lombaire.

Localisation.

4ème disque cervical	4	
6ème " cervical	5	
10ème " dorsal	1	
12ème " dorsal	3	
1er " lombaire	3	1000
2ème " lombaire	2	
3ème " lombaire	26	
4ème " lombaire	508	
5ème " lombaire	413	
1er " disque sacré	1	
2ème et 3ème disques lombaires	1	
3ème et 4ème disques lombaires	12	
4ème et 5ème disques lombaires	34	
		1013

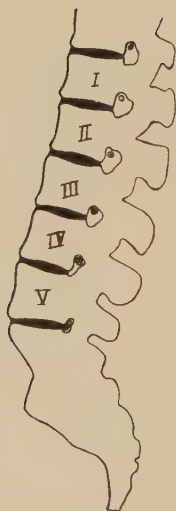


Fig. 10.

Rapport entre la grandeur du trou intervertébral et le diamètre de la racine correspondante (d'après Danforth & Wilson).

Travail physique facile comprenant principalement les individus ayant un travail sédentaire.

Examinés à ce point de vue, on trouve que :

parmi les hommes	58 % fournissent un travail dur,	28 % pour les femmes
	18 % un travail moyen,	39 %
	24 % un travail facile,	33 %

Plus de la moitié des femmes ayant à fournir un travail dur et souffrant de prolapsus étaient des infirmières.

Etant donné que chez un certain nombre de malades il semble que le prolapsus se soit produit à la suite de l'exercice d'un *sport* quelconque, on a examiné aussi ce côté du problème. On a trouvé que les sportifs étaient très faiblement représentés dans les groupes ayant un travail dur et moyen, tandis que plus du tiers des malades ayant un travail facile pratiquent du sport.

Afin de montrer *l'importance de la maladie pour la profession* du malade, nous avons étudié la durée de l'incapacité de travail avant l'opération, en la comparant au degré de dureté du travail. Nous avons ainsi trouvé que 76% de tous les malades avaient été très longtemps incapables de travailler, ce pourcentage s'élevant toutefois à 82% pour les hommes ayant à fournir un travail dur, un peu moins élevé dans les autres groupes du sexe masculin. Parmi les femmes, 75% avaient été longtemps incapables de travailler, sans répartition spéciale entre les groupes. Plusieurs malades ont été obligés de changer de profession par suite de leur maladie.

PROLAPSUS DISCAL ET TRAUMATISME

Par PER PERMIN

L'importance du traumatisme dans le prolapsus discal est indéniable. Tandis que le rôle du trauma comme facteur déclenchant les symptômes est absolument certain, il est difficile de prouver que le traumatisme est la cause primaire du prolapsus. On a prétendu que la maladie était due à une dégénération primaire du disque, le trauma n'intervenant que comme un facteur aggravateur. Mais on ne sait toutefois rien de certain sur une telle dégénération — une « dégénération » se produit normalement avec les modifications du nucléus pulposus causées par l'âge. Mais comme on l'a vu plus haut, la plupart des malades n'ont pas trente ans. Le fait aussi que ce sont surtout les malades de certaines professions qui souffrent de prolapsus, indique à notre avis une étiologie traumatique dans beaucoup de cas. Pour reconnaître un trauma comme ce que nous appelons le « *trauma causateur probable* », nous demandons en tout premier lieu qu'il

s'agisse d'un *traumatisme de prolapsus adéquat*, c'est-à-dire de telle nature et de telle force qu'il est supposé pouvoir provoquer une rupture d'annulus. Par ailleurs, il faut exiger aussi que le traumatisme soit suivi immédiatement d'un lumbago typique ou d'une lombo-sciatique. Les autres traumas rencontrés au cours de la maladie et qui, souvent, déclenchent de nouvelles crises, sont désignés *traumas secondaires* ou *occasionnels*. On a constaté que le trauma causateur remonte souvent à plusieurs années; en général il ne déclenche que des douleurs lombaires que le malade ne rapproche pas toujours de la « sciatique » qui apparaît plus tard.

Dans nos observations, nous avons trouvé chez nos premiers 400 malades des *traumas causateurs probables* dans 55% des cas; si l'on prend également les traumas causateurs possibles, on arrive à 65%. Si l'on classe les traumas causateurs probables d'après leur nature, on constate que le trauma causé par le soulèvement d'un poids lourd est de loin le plus fréquent; on le trouve dans la moitié de tous les traumas causateurs, comme on pouvait s'y attendre s'il s'agissait de connexe causal. Les douleurs lombaires se rattachent immédiatement au trauma et constituent les premiers symptômes chez un malade ayant été antérieurement absolument bien portant, celui-ci se trouvant subitement immobilisé ou s'en allant courbé en deux. Le deuxième grand groupe est constitué par les *traumas directs du siège* — par conséquent un traumatisme de compression — qui représente un quart de tous les cas. D'autres traumas adéquats du prolapsus que l'on peut accepter comme causes probables — *traumas dorsaux directs*, *traumas de torsion*, *traumas plus compliqués* — apparaissent dans un petit nombre de cas, sans répartition spéciale. Leur relevé établit qu'il n'y a guère de différence dans la fréquence de leur manifestation dans les deux sexes. De même, la nature du trauma ne semble pas avoir d'importance sur la localisation du prolapsus dans le 4^{ème} ou le 5^{ème} disque. Les *traumas secondaires* sont extrêmement courants dans les anamnèses, où une nouvelle crise est régulièrement précédée d'un de ces traumas secondaires souvent de si faible importance qu'on peut à peine parler de traumatisme — il s'agit par exemple de ramasser un livre tombé par terre, de circuler dans une voiture mal suspendue, et il est clair qu'il ne peut pas être question ici de traumatisme dans le sens prévu par la législation sur les assurances contre les accidents. Il en est autrement du traumatisme primaire — il est évident pour nous qui nous sommes occupés de ces malades pendant plusieurs années, que ce que nous appelons *traumatisme causateur probable* — un trauma adéquat du prolapsus qui déclenche les premiers symptômes du prolapsus (lumbago ou lombo-sciatique) chez un malade autrement bien portant, doit être entendu comme relevant de la loi.



Fig. 11.

ANOMALIES DE POSITION ET SYMPTOMES MOTEURS D'ABOLITION

Par ÉLISE TRUELSEN

Anomalies d'attitude.

L'altération la plus fréquente de la colonne lombaire dans le prolapsus discal est l'aplatissement de la lordose normale qui dans les cas les plus accentués peut se transformer en une légère cyphose, en position verticale ordinaire.

C'est ainsi que nous avons trouvé une *lordose lombaire aplatie, respectivement une cyphose* dans 80% en moyenne de tous les cas de prolapsus du 4^{ème} disque et dans 70% de ceux du 5^{ème} disque lombaire. La cyphose ne se trouve que dans 5,5% de nos observations (chez nos premiers 400 malades).

La *scoliose* est plus rare : nous l'avons constatée dans 34% de nos cas de prolapsus du 4^{ème} et dans 28% de ceux du 5^{ème} disque lombaire. La *convexité de la scoliose* correspond le plus souvent au côté dans lequel le malade a les douleurs et par conséquent celui où est localisé le prolapsus — mais ce n'est cependant pas une règle absolue et il n'est surtout pas rare de trouver une scoliose lombaire sinistroconvexe chez des malades souffrant de douleurs de prolapsus du côté droit. Quand il s'agit du 5^{ème} disque, on observe de plus nombreux cas de scoliose sinistroconvexe, au lieu de dextroconvexe, que l'on s'attendait à trouver. Il est possible qu'il faille chercher la *raison* de ce décalage dans le fait que la colonne lombaire normale a tendance à une faible scoliose sinistroconvexe compensant la scoliose dorsale dextroconvexe habituelle et normale.

La *scoliose isolée* avec lordose lombaire normale est rare, 3 à 8% des cas dans les différents groupes, de sorte que la combinaison scoliose + lordose aplatie donne des chiffres se rapprochant beaucoup de ceux des scolioses, à savoir 31% pour le prolapsus du 4^{ème} et 22% du 5^{ème} disque lombaire.

La *lordose aplatie seule*, non accompagnée de scoliose, apparaît dans 49% des cas et est à peu près égale pour le 4^{ème} et le 5^{ème} disque.

Sensibilité directe.

La sensibilité directe de l'apophyse épineuse est constatée avec pratiquement la même fréquence dans le 4^{ème} et le 5^{ème} disque lombaire, à savoir dans 43 et 44% des cas, respectivement. *Le plus souvent, la sensibilité directe indiquée est non seulement localisée* à l'endroit du prolapsus correspondant à l'apophyse, mais également dans une ou plusieurs adjacentes. Nous avons attaché une importance particulière au fait qu'une pression sur l'apophyse épineuse déclenche les douleurs irradiantes ou les parasthésies typiques à ce malade, fait que l'on peut parfois observer très distinctement. Il est cependant rare et ne représente chez nos malades que 4,7% des cas.

Mobilité.

La *réduction typique de la mobilité de la colonne vertébrale* dans les cas de prolapsus discal se manifeste dans la difficulté de la flexion en avant. Nous avons pu la chiffrer en demandant au malade en position verticale d'essayer de toucher le plancher du bout des doigts sans plier les genoux. On considère qu'il y a réduction de la flexion en avant lorsque les doigts sont à plus de 10 cm du sol. Ceci a été

constaté dans 76% des cas de prolapsus du 4^{ème} disque et dans 65% de ceux du 5^{ème} disque — donc ici aussi un chiffre légèrement plus élevé pour le 4^{ème}. Par ailleurs, on enregistre les cas les plus graves dans le 4^{ème} disque, puisque chez 23% de ces malades la flexion en avant est si compromise (fig. 10) que la distance entre les doigts et le sol est de plus de 45 cm, correspondant à peu près à la hauteur des genoux, fait qu'on ne trouve que dans 15% des cas du 5^{ème} disque. Une autre fixation (réduction de la flexion en arrière ou de côté) montre une différenciation similaire entre les prolapsus du 4^{ème} et du 5^{ème} disque, apparaissant dans nos observations avec 61 et 52% respectivement.

Parésies.

On a trouvé des parésies en moyenne chez 29% de nos malades du prolapsus du 4^{ème} ou du 5^{ème} disque, plus fréquentes aussi dans le 4^{ème}, avec 32%, que dans le 5^{ème} où il n'y en avait que 23%.

Les cas qui présentent le plus grand intérêt sont ceux chez lesquels on a trouvé des parésies électives. Le nombre des parésies électives est trop faible pour être exprimé en pourcentage et c'est pourquoi nous les indiquons en chiffre absolu :

Sur 196 cas de prolapsus du 4^{ème} disque lombaire, on a trouvé des parésies électives chez 25 malades (soit 12%); sur 185 cas du 5^{ème} disque, on a trouvé des parésies électives chez 28 (soit 14%).

Si l'on essaie maintenant de faire un rapprochement entre ces parésies plus localisées et le siège du prolapsus, on ne trouvera des données utilisables que pour certains groupes seulement.

C'est le cas en premier lieu de la flexion dorsale du pied ou des orteils qui comprennent 35 cas sur 53 avec parésies électives — 4^{ème} disque 18 cas = 9,2%, 5^{ème} disque 17 = 9,1%.

D'autres auteurs (*Malmros, Sjöqvist, Norlén*) ont aussi indiqué la parésie de flexion dorsale du pied, des orteils ou simplement du gros orteil comme la parésie élective la plus fréquente; mais on a trouvé une parésie dans tous ces cas de prolapsus du 4^{ème} disque; dans les observations de Norlén chez 14 malades 53 = 26%, tandis qu'il ne l'a trouvée dans aucun des 46 cas de prolapsus du 5^{ème} disque.

La parésie élective qui est ensuite la plus fréquente porte sur la flexion plantaire du pied qui se trouve atteinte dans 5 cas du prolapsus du 4^{ème} et 11 cas du 5^{ème} disque, respectivement 2,6 et 5,9% des cas.

L'innervation de la flexion dorsale du pied et des orteils est indiquée

comme ayant lieu par l'intermédiaire des 4^{ème} et 5^{ème} racines lombaires et de la 1^{ère} racine sacrale, ce qui semble bien correspondre à une compression surtout de la 5^{ème} racine lombaire dans le prolapsus du 4^{ème} disque et de la 1^{ère} racine sacrale dans celui du 5^{ème} disque, bien que l'on s'attende sans doute à une différenciation plus forte à l'avantage du prolapsus du 4^{ème}, du fait que la plus grande partie de l'innervation doit se faire par la 5^{ème} racine.

L'innervation de la flexion plantaire du pied a lieu en partie par les 4^{ème} et 5^{ème} racines lombaires, la 1^{ère} racine sacrale par le nerf péronier superficiel au groupe des péroniers, en partie par la 5^{ème} racine lombaire, les 1^{ère} et 2^{ème} racines sacrales, par le nerf tibial au groupe musculaire postérieur de la jambe qui est de loin le plus grand. Si l'on trouve fréquemment des parésies de flexion plantaire dans le prolapsus du 5^{ème} disque, c'est que l'innervation principale se fait par la 1^{ère} racine sacrale.

Atrophie.

On a constaté une atrophie des membres inférieurs dans 50% des cas de prolapsus du 4^{ème} disque et dans 41% de ceux du 5^{ème} disque. Le degré et la localisation de l'atrophie exprimés par la grandeur de la circonférence de la cuisse et de la jambe, comparée à celle de l'autre membre inférieur, ne montrent pas de répartition typique correspondant aux diverses localisations des douleurs et du prolapsus, la diminution la plus marquée dans chaque groupe affectant tantôt la cuisse, tantôt la jambe. La plus grande différence relevée était de 4 cm, elle est généralement de 1 à 2 cm.

En résumé.

On trouve aussi bien des *anomalies d'attitude* avec lordose aplatie et scoliose, restriction de la mobilité, diminution de la flexion en avant ou autre fixation, particulièrement fréquentes dans les prolapsus du 4^{ème} ou du 5^{ème} disque, dans tous les cas un peu plus fréquentes dans le prolapsus du 4^{ème} que du 5^{ème}. Les chiffres sont toutefois si élevés dans les deux groupes et les divergences si faibles, relativement, que l'on ne peut pas, dans un cas particulier, s'appuyer sur certains des symptômes ou sur le syndrome complet, pour localiser le prolapsus.

Nous n'avons pas non plus trouvé de point d'appui pour diagnostiquer le siège de la maladie — comme d'autres — dans la parésie de la flexion dorsale du pied ou des orteils; d'après nos observations, il convient d'attacher une plus grande importance à la parésie de flexion plantaire qui — bien que rare — dans plus de 2/3 des cas indiquait un prolapsus du 5^{ème} disque.



Fig. 12.

TROUBLES DE LA SENSIBILITÉ ET MODIFICATION DES RÉFLEXES DANS LES CAS DE PROLAPSUS

Par TORBEN FOG

Des troubles de la sensibilité, sous forme de paresthésies ou d'hypoesthésies, ont été observés dans 75% de nos premiers 400 cas — des paresthésies dans plus de 67% et des hypoesthésies dans 50%. *Paresthésies.* Celles-ci sont vraisemblablement, dans la plupart des cas, neurogènes, radiculaires, c'est-à-dire qu'elles sont provoquées par l'irritation exercée par le prolapsus sur la racine rachidienne en question et elles devraient donc se rattacher au dermatome innervé par la racine. Il s'ensuit théoriquement que l'on devrait pouvoir, d'après la localisation de la paresthésie, déterminer le siège du prolapsus, tout comme *Norlén* utilisait la localisation des douleurs. Dans la pratique, les choses ne sont cependant pas aussi simples, d'une part parce que certaines racines empiètent les unes sur les autres dans le même dermatome, d'autre part parce que le prolapsus peut irriter plusieurs racines et qu'il peut enfin se déplacer dans le canal rachidien. D'après le schéma des dermatomes de *Keegan* (fig. 12) que nous utilisons,

on voit que le dermatome L5 est situé sur la partie antérieure de la jambe, suivant le dos du pied en direction du gros orteil, tandis que le côté extérieur de la jambe, de la cheville, le côté du pied et les orteils latéraux se trouvent dans le dermatome S1. Dans ces observations, on a retrouvé un rapport entre les paresthésies et les dermatomes dans 2/3 des cas, à savoir 66% de prolapsus du 4^{ème} disque et 69% de ceux du 5^{ème} disque.

196 malades souffrant de prolapsus du 4^{ème} disque ont été examinés. Parmi ceux-ci 145 étaient atteints de paresthésies et chez 99 il a été possible de les répartir suivant les dermatomes avec assez de certitude, tandis que les observations médicales étaient insuffisantes pour 46 :

L5 seulement	30 malades
S1 seulement	24 „
L5 + S1	40 „
L4 + L5 + S1	3 „
L5 + plusieurs racines sacrales	1 „
L4 seulement	1 „
Appréciation incertaine	46 „

Dans le prolapsus du 4^{ème} disque lombaire, on trouve donc, avec une fréquence sensiblement identique, des paresthésies dans L5 seulement et dans S1 seulement; les paresthésies simultanées dans L5 et S1 sont toutefois plus fréquentes. L'essentiel est cependant que le *dermatome L5 est représenté isolément ou en combinaison avec d'autres racines dans pas moins de 73% des cas* (74 malades), ce qui indique qu'il y a beaucoup de chance qu'il s'agisse d'un prolapsus du 4^{ème} disque lorsque les paresthésies sont situées sur la partie antérieure de la jambe et le dos du pied.

Parmi les 186 malades souffrant de prolapsus du 5^{ème} disque lombaire, 116 avaient des paresthésies. 80 de ceux-ci ont pu être répartis suivant les dermatomes :

S1 seulement	60 malades
L5 + S1	7 „
L4 + L5 + S1	7 „
L5 seulement	4 „
Appréciation incertaine	36 „

Dans les prolapsus du 5^{ème} disque, les paresthésies se trouvent uniquement dans le dermatome S1 dans 75% des cas, ce dermatome étant représenté dans 95% (76 malades). L5 n'est représenté que dans 18% en tout (15 cas).

La répartition par dermatome des paresthésies semble donc bien

indiquer qu'elles sont radicalement conditionnées dans les prolapsus discaux. Il est d'ailleurs très probable que le prolapsus siège dans le 4^{ème} disque lorsqu'il y a des paresthésies dans le dermatome L5, tandis que les paresthésies S1 indiqueraient plutôt un prolapsus du 5^{ème} disque.

Hypoesthésies. On a trouvé des hypoesthésies chez 99 malades sur les 196 cas dans lesquels le prolapsus du 4^{ème} disque a été vérifié :

L5 seulement	7 malades
L5 + S1	24 „
L5 + plusieurs racines sacrées	3 „
L4 + L5	2 „
S1 seulement	59 „
tous les segments sacrés	2 „
toute la jambe	2 „

Tandis que les modifications isolées dans le dermatome L5 sont rares, l'hypoesthésie isolée dans S1 est fréquente (60% des cas). Le dermatome S1 est représenté dans pas moins de 80% des cas, tandis que L5 n'est représenté que dans 36%. Les prolapsus du 5^{ème} disque montrent que sur 186 malades, il y avait de l'hypoesthésie chez 93 :

S1 seulement	69 malades
L5 + S1	6 „
L4 + S1	1 „
segments sacrés	7 „
L5 seulement	1 „
toute la jambe	6 „
impossible à apprécier	3 „

Le dermatome S1 apparaît ainsi chez 83 sur 93 malades, c'est-à-dire dans 89% des cas, le dermatome L5 seulement dans 7 sur 93 cas. Il semble donc que le dermatome S1 soit très fréquemment représenté tant dans le prolapsus du 4^{ème} que du 5^{ème} disque lombaire. L'hypoesthésie n'a donc pas une grande importance pour le diagnostic de la localisation. Les modifications du dermatome L5 sont plus rares, mais quand on les rencontre, il y a beaucoup de chance qu'il s'agisse d'un prolapsus du 4^{ème} disque.

MODIFICATIONS DES RÉFLEXES

Par TORBEN FOG

On a constaté des modifications de réflexes dans 219 des 400 cas — sur 382 cas de prolapsus des 4^{ème} et 5^{ème} disque, il y en avait 207, ce qui correspond ainsi à environ 55% des cas. Les modifications de

réflexes semblent plus fréquentes dans le prolapsus du 5^{ème} disque, 112 sur 186 malades souffrant de ce prolapsus ayant des modifications contre 95 sur 196 du 4^{ème} disque.

Réflexe achilléen. Ce réflexe a principalement son arc de réflexe par la lère racine sacrale, et devrait donc théoriquement être plus fréquemment atteint dans les prolapsus du 5^{ème} disque.

L'aréflexie achilléenne unilatérale a été constatée dans 23 % de toutes les observations, dans 30% de prolapsus du 4^{ème} et 58% du 5^{ème} disque, ce qui revient à dire que l'aréflexie achilléenne unilatérale semble indiquer un prolapsus du 5^{ème} disque dans le rapport de 2 à 1. Il est assez curieux que l'on n'ait constaté un *réflexe achilléen diminué unilatéralement* que dans 17% des prolapsus du 5^{ème} disque, mais dans 19% des prolapsus du 4^{ème} disque. Au total, on trouve un réflexe achilléen diminué ou aboli dans 75% des cas vérifiés de prolapsus du 5^{ème} disque lombaire et dans 49% de ceux du prolapsus du 4^{ème}. *L'aréflexie achilléenne bilatérale* se trouve dans les cas de gros prolapsus avec douleurs bilatérales — chez 10% du 4^{ème} et 8% des prolapsus du 5^{ème} disque. Dans ces deux derniers groupes, le nombre supérieur pour le prolapsus du 4^{ème} disque ne correspond pas aux faits anatomiques, mais s'explique probablement du fait du glissement du prolapsus du 4^{ème} disque, souvent constaté à l'opération qui fait que la compression atteint principalement S1. Elle peut être due aussi à une technique d'examen défectueuse de la part des différents examinateurs; il convient enfin de citer que l'arc réflexe passe principalement par L5 chez un grand nombre d'individus.

Le *réflexe patellaire* n'a d'intérêt que dans les prolapsus du 3^{ème} disque lombaire, l'arc du réflexe passant principalement par L4. Sur nos 11 cas, le réflexe n'a été influencé avec certitude que chez deux. Dans les prolapsus du 4^{ème} et du 5^{ème} disque, on a trouvé dans quelques rares cas un réflexe patellaire diminué avec un chiffre nettement plus élevé pour le 4^{ème}, ce à quoi on devait d'ailleurs s'attendre.

Dans un certain nombre de cas, cette modification paraît cependant sans importance et est due à d'autres causes.

Troubles sphinctériens. Dans les gros prolapsus qui compriment toute la queue de cheval, il se manifeste évidemment des troubles — sphinctériens massifs comme dans les tumeurs — ordinairement rétention d'urine, dans certains également des selles. Les modifications légères sont plus fréquentes. On a constaté des troubles sphinctériens dans 36 de nos premiers 400 cas, soit 9,6%. Ils sont plus fréquents dans les prolapsus du 5^{ème} disque, 19 sur 186, contre 19 sur 196 du 4^{ème} disque, ce qui correspond ainsi à 11 et 6%. Par contre, ils existaient aussi dans 5 des 11 cas de prolapsus du 3^{ème} disque lombaire, ce

qui indique que ces prolapsus sont généralement très gros. Les symptômes ont ordinairement peu de durée et disparaissent rapidement après l'opération.

Des *troubles génitaux* ont été signalés dans 7 cas. Ils sont donc rares et tout comme les symptômes sphinctériens se manifestent notamment dans les cas de prolapsus bilatéraux, disparaissant ordinairement quelques mois après l'opération.

PROLAPSUS DE DISQUE ET LIQUIDE CÉPHALO-RACHIDIEN

Par THOMAS CLAUDIUS

Parmi nos 400 premiers malades, le liquide céphalo-rachidien a été examiné chez 329. Dans le Service Neurochirurgical de l'Hôpital de l'Université, nous considérons, pour des raisons d'ordre pratique, qu'un liquide céphalo-rachidien est normal lorsqu'il contient au maximum : 10/3 cellules, globuline 1, albumine 10, bien que nous sachions pertinemment que ces limites ne peuvent absolument pas être considérées comme sûres ou généralement admises — surtout en ce qui concerne l'albumine, la limite étant un peu faible.

On n'a trouvé un nombre augmenté de cellules que dans 4% (12 cas). Dans l'un de ceux-ci, on découvrit à l'opération une arachnoïdite distincte, dans un autre il y avait une formation marquée de tissu granulé autour du prolapsus. Dans les 10 autres cas, on n'a pas trouvé l'explication de l'augmentation du nombre des cellules qui était d'ailleurs faible — entre 10/3 et 31/3; dans tous ces cas, il y avait une légère augmentation d'albumine imputable vraisemblablement aux modifications des conditions de la circulation autour de la racine incarcérée.

De l'hyperalbumine (> 10) a été observée chez 160 malades se répartissant comme suit :

Albumine	>10—20	>20—30	>30—40	>40—50	>50—70	100	175
% des 329 cas	32 %	10 %	2,5 %	2,5 %	1,6 %	0,2 %	0,2 %

L'un des cas avec albumine 175 avait un nombre de cellules de 31/3 et il y avait une formation distincte de tissu granulé autour du prolapsus. Une ponction lombaire au-dessous du prolapsus montra dans un cas un bloc partiel avec cellules 2/3, glob. 1-2, albumine 22. Dans un cas, on trouva un bloc complet à l'épreuve de Queckenstedt avec liquide normal au-dessous d'un gros prolapsus du 1^{er} disque

lominaire. Si l'on établit un rapport entre l'hyperalbumine et la durée de l'anamnèse, on trouve une tendance à une légère augmentation du taux de l'albumine dans les cas à longue anamnèse :

Anamnèse	<1 an	>1—2 ans	>2—5 ans	>5—10 ans	>10 ans
% de tous les cas	12 %	19 %	15 %	22 %	32 %

En résumé, il convient toutefois de relever que les examens du liquide céphalo-rachidien ne présente pas d'importance pour le diagnostic du prolapsus discal et qu'on peut parfaitement l'omettre lorsque l'anamnèse et les trouvailles objectives sont typiques. Par contre cet examen présente de l'intérêt lorsqu'il s'agit d'éliminer d'autres maladies dont la symptomatologie est analogue, notamment dans le cas de certaines tumeurs rachidiennes, de métastases des vertèbres et d'autres dans lesquelles les symptômes diffèrent toutefois suffisamment de ceux du prolapsus pour éveiller les soupçons. Il faut relever cependant que certaines tumeurs rachidiennes peuvent provoquer exactement le même tableau de maladie que le prolapsus du disque, mais elles sont si rares qu'il n'est sans doute pas justifié d'exposer les autres malades souffrant du prolapsus discal aux inconvénients et aux risques de la ponction lominaire. Il en est évidemment autrement dans les cas où l'on observe le syndrome proprement dit de la queue de cheval. *Broager* a trouvé en tout 20 malades parmi nos premiers 1000 cas qui présentaient ce syndrome; mais même chez ceux-ci, la quantité d'albumine est généralement assez inférieure à celle observée dans les cas de tumeurs et particulièrement de neurinomes.

NATURE ET DURÉE DES TRAITEMENTS ANTÉRIEURS

Par PER PERMIN

Parmi nos premiers 600 malades, 10% n'avaient pas été hospitalisés précédemment pour leur maladie, tandis que 50% avaient fait un, 24% deux, 10% trois et 6% plus de trois séjours à l'hôpital. La durée du stage à l'hôpital pour les malades antérieurement hospitalisés a été dans un peu plus de la moitié des cas 3 mois ou plus, ce qui constitue évidemment une grosse charge économique pour le malade.

Nous avons essayé de dresser un tableau indiquant les traitements antérieurs auxquels ont été soumis nos premiers 600 malades. Celui-ci ne peut évidemment fournir que des renseignements approximatifs et ses données doivent sans doute être considérées comme des chiffres minima :

traitement physiothérapique	507
vitamines	118
chiropraticien	36
rayons X	28
charlatan, homme ou femme	14
extension	14
corset d'étoffe	16
couche ou corset de plâtre	13
blocage du grand sympathique	17
chaussures orthopédiques	7
opération d'Albee	2

Il a été fait à la majorité des malades des « piqûres » et il leur a été ordonné des « médicaments » qu'il n'est pas possible de spécifier. Le nombre des malades soignés par des chiropraticiens ou des charlatans est certainement trop faible. Si nous disons traitement physiothérapique au lieu de physiurgique, c'est en toute connaissance de cause, la plupart des malades ayant pris des bains et reçu du massage, mais très peu d'entre eux ayant été soignés par un véritable physiurge.

MODIFICATIONS RADIOLOGIQUES DANS LE PROLAPSUS DISCAL

Par ARNE ANDERSEN

Les examens radiographiques de la colonne lombaire n'ont eu jusqu'à présent qu'une faible importance pour le diagnostic même du prolapsus du disque et ont présenté essentiellement de l'importance au point de vue du diagnostic différentiel, abstraction faite de quelques cas où le prolapsus a été directement visible sur la radiographie par suite d'une calcification. On a aussi envisagé la question d'un aplatissement éventuel du disque correspondant au prolapsus et du rétrécissement qui s'ensuit de l'espace intervertébral, mais ces examens n'ont eu aucune valeur du fait qu'ils ont tous été basés sur une pure appréciation de la hauteur de l'espace intervertébral. C'est pourquoi nous avons remis la question à l'étude pour essayer d'élaborer une méthode de mesure plus exacte afin de pouvoir déterminer la hauteur de l'espace intervertébral.

Manière de procéder.

Les mesures ont toutes été prises sur des radiographies latérales de la colonne lombaire faites comme d'ordinaire. Sur une radiographie de côté, les différents espaces intervertébraux varient fortement de

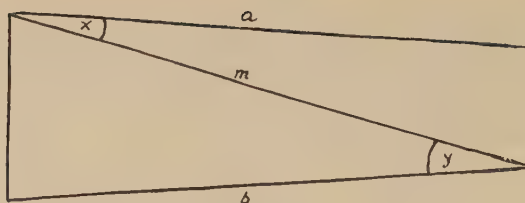


Fig. 13.

Représentation schématique d'un espace intervertébral. On obtient la superficie en mesurant les lignes a , b et m , ainsi que les angles x et y .

forme et de dimension et la hauteur diffère suivant l'endroit d'où l'on prend la mesure et ne peut donc être mesurée directement. C'est pourquoi j'ai préféré mesuré toute la surface limitée par les 4 « coins » de l'espace intervertébral.

Cette surface schématiquement représentée à la figure 13 dépend toutefois non seulement de la hauteur de l'espace intervertébral, mais aussi de sa largeur, c'est-à-dire de la distance entre la hauteur en avant et la hauteur en arrière et j'ai décidé d'éliminer l'incertitude des mesures venant du fait que cette largeur n'est pas une grandeur constante, en divisant le chiffre de la superficie par la largeur déterminée comme la dimension moyenne entre a et b .

La surface elle-même est mesurée en la divisant par la ligne m en deux triangles, la superficie de chacun de ceux-ci pouvant maintenant être déterminée en mesurant les lignes a , b et m , ainsi que les angles x et y . La donnée obtenue est divisée comme dit plus haut par un nombre moyen entre a et b et la grandeur que l'on obtient est l'expression de la hauteur moyenne de l'espace intervertébral. Celle-ci est maintenant comparée à la donnée correspondante de l'espace intervertébral sus-jacent, en établissant un rapport entre eux. Le quotient ou l'indice ainsi obtenu — comme je l'appellerai par la suite — peut être utilisé maintenant comme base de comparaison.

Pour déterminer la valeur normale de l'indice, on a procédé au calcul de l'indice de tous les 5 espaces intervertébraux en question sur des sujets de contrôle obtenus par la prise de radiographies latérales de la colonne lombaire d'une série de malades qui n'ont jamais présenté les symptômes de prolapsus discal.

Sujets de contrôle.

Ce matériel comprend en tout 44 malades (19 hommes et 25 femmes) répartis dans les classes d'âges de 19 à 52 ans comme indiqués sur le diagramme de la fig. 14.

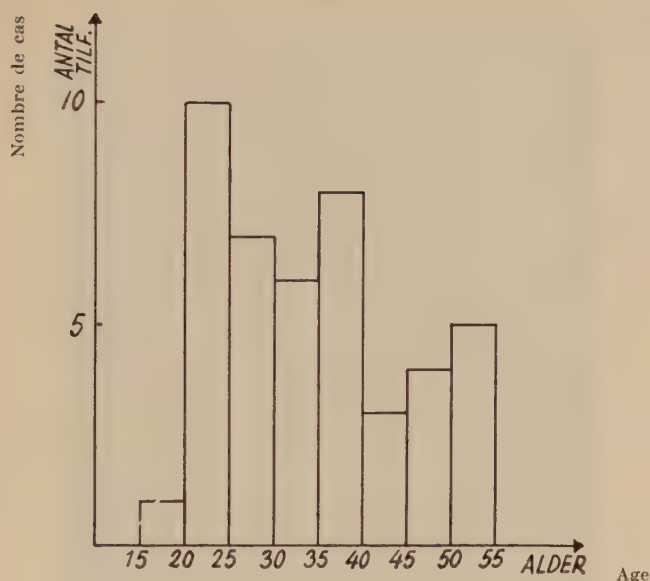


Fig. 14.

Répartition des sujets de contrôle dans les différentes classes d'âge.

La valeur des indices des 4^{ème} et 5^{ème} espaces intervertébraux est indiquée sur les diagrammes des fig. 15 et 16. On voit ici que l'indice du 4^{ème} espace intervertébral est toujours $+ ou = 1$, ce qui signifie que cet espace intervertébral est toujours plus haut ou aussi haut que le 3^{ème} et en tout cas *jamais* moins élevé que celui-ci. En ce qui concerne le 5^{ème} espace intervertébral, la donnée inférieure de l'indice est 0,80 et dans 64% des cas l'indice est au-dessous de 1; dans ces cas, le 5^{ème} espace intervertébral est moins élevé que le 4^{ème} et c'est seulement quand le rétrécissement est si marqué que l'indice tombe à moins de 0,80 qu'on peut le considérer comme étant pathologique. Le résultat de l'examen du matériel de contrôle indique donc que dans tous les cas où l'indice est inférieur à 1 il y a rétrécissement pathologique de l'espace intervertébral en question excepté en ce qui concerne le 5^{ème} espace intervertébral où l'indice doit être inférieur à 0,80 pour que le rétrécissement puisse être considéré comme pathologique.

Observations.

Ces données normales ont ensuite été prises comme bases dans l'examen de nos propres observations qui comprennent 269 cas de prolapsus discal lombaire vérifiés à l'opération.

Ceux-ci se répartissent comme suit :

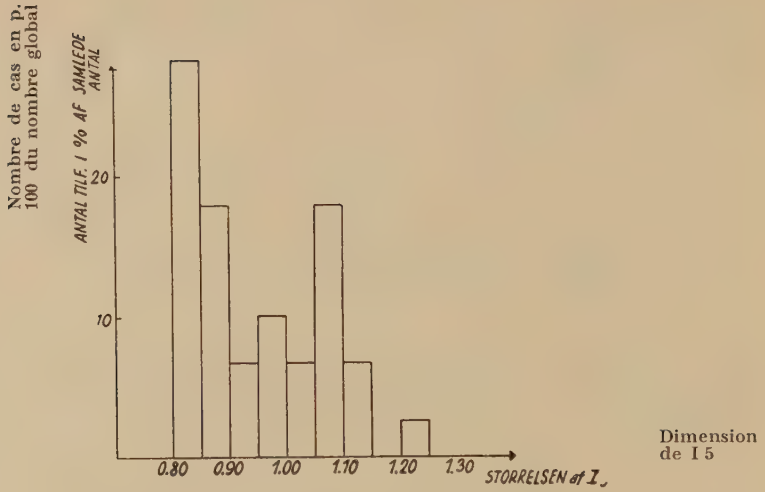


Fig. 15.

Diagramme indiquant la valeur de l'indice du 5ème espace intervertébral (I₅) tel qu'il se répartissait chez les sujets de contrôle.

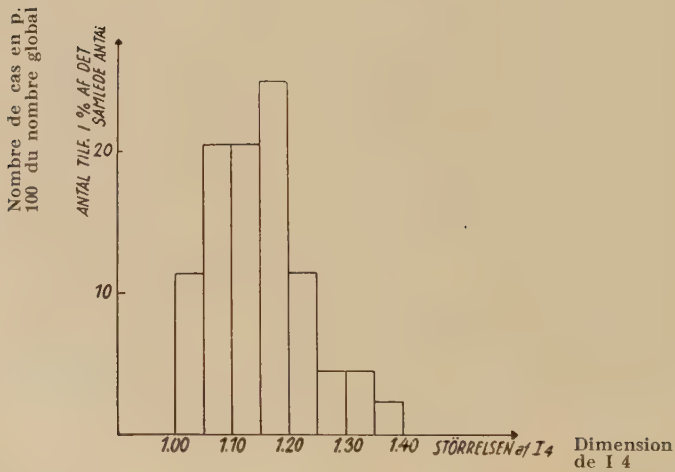


Fig. 16.

Diagramme indiquant la valeur de l'indice du 4ème espace intervertébral (I₄) tel qu'il se répartissait chez les sujets de contrôle.



Fig. 17.

Rétrécissement du 5^{ème} disque lombaire dans un cas de prolapsus discal total.



Fig. 18.

Rétrécissement des 4^{ème} et 5^{ème} disque lombaires avec bordure d'ostéophytes dans un cas de prolapsus discal.

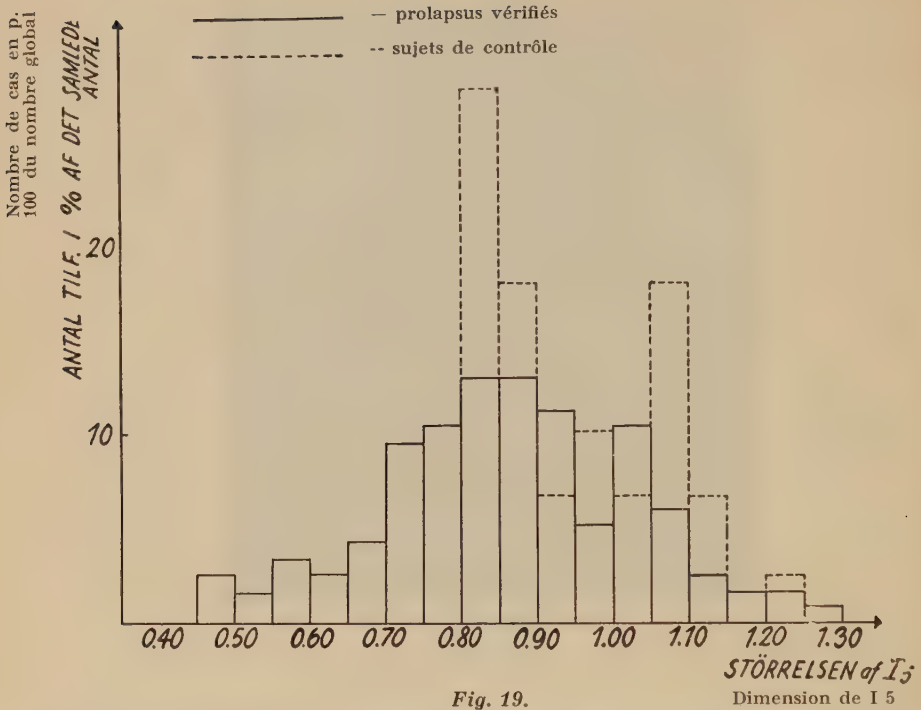


Fig. 19.

Diagramme indiquant la valeur de l'indice du 5ème espace intervertébral (I_5), tel qu'il se répartissait dans 116 cas de prolapsus du 5ème disque lombaire. A titre de comparaison, diagramme correspondant pour les sujets de contrôle (-----).

Espace intervertébral	1	2	3	4	5
Nombre de cas	2	0	10	141	116

De loin la plupart des cas (96%) sont ainsi localisés dans les 4ème et 5ème espaces intervertébraux et ce sont donc essentiellement les résultats obtenus là qui sont intéressants.

La valeur des indices de ces deux espaces intervertébraux est indiquée sur les diagrammes des fig. 19 et 20.

En ce qui concerne le 4ème espace intervertébral, on verra que dans la moitié des cas (50,4%), l'indice est au-dessous de la limite normale et il y a donc dans ces cas un rétrécissement de l'espace intervertébral. Pour le 5ème espace intervertébral où la limite normale était de 0,80, l'indice est dans 34,5% des cas inférieur à cette limite et il y a donc dans ces cas un rétrécissement pathologique. Sur les 10 cas du 3ème espace intervertébral, on a trouvé également un rétrécissement dans 5, soit 50%. Pour les 2ème et 1er espaces intervertébraux, il n'est pas possible de donner une appréciation en se basant sur les présentes observations. Si l'on considère les 5ème, 4ème et 3ème espaces interverté-

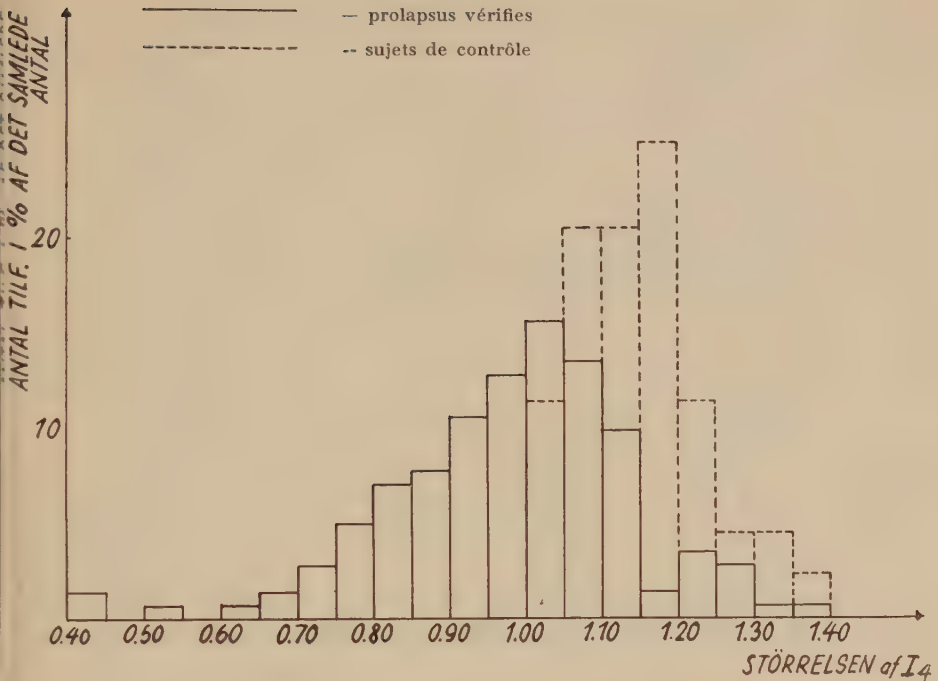


Fig. 20.

Dimension de I 4

Diagramme indiquant la valeur de l'indice du 4ème espace intervertébral (I₄) tel qu'il se répartissait dans 141 cas de prolapsus du 4ème disque lombaire. A titre de comparaison, diagramme correspondant pour les sujets de contrôle (-----).

braux ensemble, on constate un rétrécissement dans environ 43% des cas.

Le résultat des mesures effectuées est donc que dans près de la moitié des cas, on a constaté un rétrécissement de l'espace intervertébral correspondant au prolapsus.

La question suivante qui se pose est celle de savoir si les rétrécissements observés sont dus dans tous les cas à des prolapsus discaux ou s'ils peuvent être dus dans certains cas à d'autres maladies ou anomalies de la colonne existant simultanément. Pour élucider cette question, nous avons indiqué au tableau suivant toutes les modifications radiographiques trouvées dans l'examen des observations.

Schéma de toutes les modifications radiographiques trouvées dans les observations des malades.

Spondylose déformante	15 cas
Spondylose déformante au 1 ^{er} degré (début de formation d'exostose)	22 „

Spondylose déformante localisée (correspondant au prolapsus)	15 cas
Spondylolisthèse	1 "
Colonne aplatie (redressement de lordose)	27 "
Scoliose de la colonne lombaire	22 "
Spina bifida	14 "
Îlots cartilagineux de Schmorl	10 "
Calcification du disque	4 "
Lombalisation de la 1ère vertèbre sacrale	8 "
Sacralisation de la 5ème vertèbre lombaire	3 "
Séquelles de fracture du corps vertébral	5 "
Fracture de l'apophyse articulaire	2 "
Fracture de l'apophyse transverse	1 "
Maladie de Baastrup	2 "
Rétrécissement visible de l'espace intervertébral correspondant au prolapsus	35 "

Sur les 15 cas de spondylose déformante, il n'y en avait aucun d'assez grave pour pouvoir vraisemblablement causer le rétrécissement d'un ou de plusieurs espaces intervertébraux. Il en est de même, à un degré encore plus marqué des 22 cas de spondylose déformante débutante qui doit être considérée comme un phénomène purement secondaire survenu à la suite de la maladie du disque qui l'a provoquée. En d'autres mots, la spondylose est une conséquence du prolapsus et ne peut donc être considérée comme la cause du rétrécissement. Il est d'ailleurs assez curieux que l'on n'ait trouvé une telle spondylose déformante localisée que dans 15 sur 169 cas de prolapsus discal lombaire, celui-ci se distinguant ainsi du prolapsus discal cervical qui, comme l'a démontré *Broager*, est presque toujours accompagné de spondylose déformante localisée.

On a observé une sacralisation de la 5ème vertèbre lombaire dans 3 cas, ce qui est supposé provoquer un rétrécissement du 5ème espace intervertébral; dans l'un de ces 3 cas, le prolapsus siégeait toutefois aussi dans le 5ème disque, tandis que dans les deux autres, il était plus haut et il n'y a donc qu'un seul cas de sacralisation de la 5ème vertèbre lombaire correspondant à un prolapsus du 5ème disque; qui présente de l'importance comme cause éventuelle du rétrécissement constaté.

On a trouvé un spina bifida dans 14 cas, ce qui n'est pas un chiffre plus élevé que celui auquel on arrive dans l'examen de n'importe quel matériel normal.

Il y avait des îlots cartilagineux de Schmorl dans 10 cas, ce qui prouve bien qu'il n'y a aucun rapport entre ceux-ci et les prolapsus discaux proprement dits.

Enfin, on voit que dans 35 cas seulement, il a été possible d'observer directement, sans effectuer de mesure spéciale, un rétrécissement de

l'espace intervertébral correspondant au prolapsus, tandis qu'en appliquant la méthode de mesure élaborée, il a été possible de démontrer le rétrécissement dans 116 cas.

Il a été ensuite procédé à un examen pour déterminer comment les cas de rétrécissement se répartissent entre les diverses catégories d'âges. Il apparaît que chez les malades de moins de 30 ans, il y a rétrécissement dans 31% des cas, mais chez ceux de plus de 50 ans dans 51%. Les cas de rétrécissement semblent donc être beaucoup plus fréquents chez les personnes âgées que chez les jeunes. On peut, semble-t-il, rapprocher ce fait de la durée de l'anamnèse qui est généralement courte chez les jeunes et beaucoup plus longue chez les personnes plus âgées.

Pour étudier ce problème de plus près, nous avons passé en revue tous les cas de prolapsus discaux dans les classes d'âges de 35 à 40 ans. Il apparaît qu'avec une anamnèse de moins d'un an il y a 30% de rétrécissement, tandis qu'il y en a 46% avec une anamnèse de plus de 5 ans. Les cas de rétrécissement semblent donc augmenter avec la durée de l'anamnèse. Si l'on examine le groupe mentionné plus haut des malades de plus de 50 ans, on constate qu'il y a concordance et que parmi ceux dont l'anamnèse avait une durée de plus de 5 ans, il y avait rétrécissement dans 65% des cas et parmi les autres seulement dans 27%. Ceci indique que ce n'est pas l'âge en soi mais, par contre, la durée de l'anamnèse qui est d'importance décisive dans la question du rétrécissement de l'espace intervertébral.

LE PROLAPSUS DISCAL LOMBAIRE D'UN POINT DE VUE PHYSIURGIQUE

Par EGILL SNORRASON

Lorsqu'au cours des examens journaliers qu'ils sont appelés à effectuer de malades ayant des douleurs lombaires ou des douleurs dans les membres inférieurs, les physiurges doivent établir s'il *peut* éventuellement s'agir de prolapsus discal lombaire, ils ne se bornent pas à utiliser la technique d'examen purement physiurgique, il la combine à un examen médical, neurologique, orthopédique ou autre pouvant être nécessaire. Les malades souffrant de douleurs lombaires ou de douleurs dans les membres inférieurs sont enclins à les considérer comme étant de nature rhumatismale et les physiurges ont la possibilité de diagnostiquer les prolapsus discaux à un stade précoce.

Le but de notre étude est d'établir s'il est possible, par le *seul*

examen physiurgique, de poser le diagnostic : prolapsus discal lombaire — et si les modifications physiurgiques peuvent être utilisées pour poser le diagnostic du niveau éventuel du prolapsus.

Les examens concernant la forme et la mobilité de la colonne, ainsi que les parésies et les atrophies des membres inférieurs dans les cas de prolapsus vérifiés à l'opération, ont déjà été décrits autre part dans cette étude et je me bornerai ici à passer en revue les modifications musculaires et leur rapport avec les symptômes neurogènes.

Comme l'a établi *J. Helweg* en 1920 dans sa thèse sur la sciatique et comme il l'a si justement relevé depuis, il se forme dans la musculature, à la suite de fonction accrue, des « myopathies de fonction » bien limitées, palpables, que nous appelons maintenant myoses. D'après *Helweg* tous les cas de sciatique s'expliquent en partant de myoses « *primaires* » par suite d'une fonction modifiée — accrue — des muscles (les myopathies dites « *e labore* »). Ces myoses primaires, conditionnées par la fonction, exerçant une pression sur les vaisseaux et les nerfs, provoquent l'apparition de douleurs, de troubles trophiques et neurogènes sous forme d'ischémie, atrophie, troubles des réflexes, symptômes de Lasègue, paresthésies et parésies.

Cependant toutes les myoses ne peuvent être caractérisées de primaires; les modifications musculaires entraînées par une arthrose coxale, une fracture de la colonne, doivent être considérées comme des myoses *secondaires*; la statique est modifiée, la musculature tendue anormalement, ce qui provoque l'apparition des myoses *secondaires*. Ce sont bien des « myopathies de fonction » *d'Helweg*, mais elles sont secondaires par rapport à une autre maladie — et non primaires comme le conçoit *Helweg*.

Dans les prolapsus discaux lombaires, les modifications musculaires de la région lombaire et des membres inférieurs sont secondaires ainsi que l'a relevé *Sv. Clemmensen*. Elles sont dues à des douleurs dans le dos et les membres inférieurs qui conduisent le malade à la fixation, c'est-à-dire que les myoses apparaissent secondairement, sur le compte de la statique modifiée du dos et des jambes pour éviter les douleurs.

Si l'on compare des observations de malades souffrant de la lombosciatique avec des myoses de fonction primaires dans la région lombaire, les cuisses et les membres inférieurs — comme *Helweg* les a décrites de façon si caractéristique — avec un cas où les myoses sont secondaires par suite de spondylose déformante, d'arthrose coxale ou de prolapsus discal lombaire (fig. 21), on constate que la localisation des myoses est identique dans toutes les observations — mais que seul le mécanisme de déclenchement diffère. Il est donc impossible

de se baser sur le seul diagnostic physiurgique, notamment lorsqu'il s'agit de déterminer le niveau du prolapsus.

La théorie d'*Helweg* sur les symptômes de la sciatique établit que tous les symptômes vasculaires et neurogènes peuvent s'expliquer comme une conséquence des « myopathies de fonction dans les régions

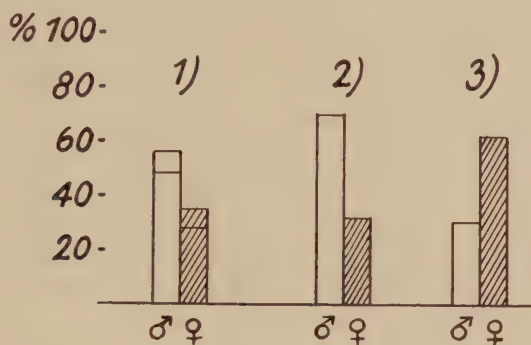


Fig. 21.

Répartition en p. 100 d'après le sexe pour les différentes séries d'observations.

- 1) prolapsus discal 212 malades
 2) Observations de J. Helweg 550 „
 3) Observations de la Clinique de Rosenvænget 47 „

Rapport entre la localisation des myoses chez les malades souffrant respectivement de prolapsus et d'arthrose, myoses dans la région lombaire et les muscles des membres inférieurs.

	erect. lomb. %	carré lomb. %	moyen fessier %	grand fessier %	fléchis. fémoral %	triceps sural %	Nombre de malades
+ prolapsus disc.	40	26	56	27	15	38	208
+ „ „	45	21	60	20	14	39	122

traversées par le nerf sciatique, respectivement celles qu'il innerve ». La cause des douleurs sciatiques dans les maladies nerveuses telle que le prolapsus et le tumeur du système nerveux central est due au fait que l'« organe kinétique » — la musculature — ne reçoit pas suffisamment d'impulsions d'où il résulte la formation de myopathie d'inactivité; celle-ci conduit à une « insuffisance passive » des muscles du jarret sous forme de tension et de transformation ischémique. Les myoses ainsi formées entraînent statiquement d'autres myoses et il s'ensuit douleurs, ischémie, symptômes de Lasègue, troubles des réflexes, atrophie, parasthésies et parésies.

Si l'on se base sur ce qui a été dit plus haut, ce point de vue doit

Fig. 22 A.

Répartition en p. 100 du symptôme de Lasègue dans les différentes localisations.

Disque interv. lombaire	+ Lasègue du côté droit			+ Lasègue du côté gauche	
	Nombre de malades	Nombre de malades	p. 100	Nombre de malades	p. 100
D. i. l. IV. gauche	47	9	20	29	65
„ IV. droit	39	24	60	6	15
„ IV. bilat.	28	14	54	11	42
D. i. l. V. gauche	38	8	20	25	63
„ V. droit	28	12	46	1	4
„ V. bilat.	28	8	30	8	30

Fig. 22 B.

Répartition en p. 100 du symptôme de Lasègue dans différentes localisations du prolapsus discal 1) du même côté, 2) des deux côtés, 3) du côté opposé et 4) négatif :

	paramédians d. i. l.				latéraux d. i. l.			
	1) %	2) %	3) %	4) %	1) %	2) %	3) %	4) %
D. i. l. IV. gauche	50	15	0	35	44	22	0	34
„ IV. droit	50	13	3	34	60	0	0	40
„ IV. bilat.	22	30	0	48	50	50	0	0
D. i. l. V. gauche	50	19	2	29	55	0	0	45
„ V. droit	37	0	5	58	64	0	0	36
„ V. bilat.	34	14	0	52	0	0	0	0
Moyenne	41	16	2	38	45	12	0	26

Fig. 23.

	Malades	+ Lasègue		+ Paresthésies	
		malades	p. 100	malades	p. 100
Clinique de Rosenvænget ♂	18	3	16	6	33
„ „ ♀	29	1	3	6	16
D. i. l. ♂	126	74	60	84	67
„ „ ♀	82	48	60	56	70

être caractérisé comme assez unilatéral — et les myoses secondaires découlant des prolapsus discaux offrent à cet égard une excellente documentation.

Parmi les premiers 400 malades opérés pour prolapsus, 212 en tout — 128 hommes et 84 femmes — ont été examinés à la Clinique de Physiurgie de l'Hôpital Militaire avant l'opération qui permit de véri-

fier le diagnostic. La répartition par sexe correspond bien en pourcentage aux observations d'*Helweg* — mais pas aux données obtenues par l'analyse de ces cas débutants dans une clinique physiurgique ambulante des Caisses de Maladies¹ (fig. 21). En ce dernier endroit, il y avait 62% de femmes et 38% d'hommes, ce qui est dû sans doute au fait que les femmes ont le temps et l'occasion de suivre un traitement ambulant dans les cas aigus; dans les cas chroniques, la maladie est si invalidisante que les hommes sont obligés de se faire soigner pour pouvoir continuer à travailler.

Le phénomène de Lasègue est généralement considéré comme un symptôme cardinal de la sciatique — qu'il soit tenu comme étant de nature musculaire ou neurogène; si on l'exécute correctement avec extension passive de la hanche sans rotation vers l'intérieur, en position couchés, on trouve le symptôme de Lasègue positif du même côté que le prolapsus dans 57% des cas et dans le côté opposé au prolapsus dans 15% quand il s'agit de prolapsus unilatéral (tableau 22 A); il est caractéristique que les prolapsus paramédians donnent plus rarement une réaction de Lasègue positive, c'est-à-dire douleurs au-dessous d'un angle de 50°, que les prolapsus latéraux (tableau 22 B). Ceci indique peut-être que ce phénomène est dû à une affection des racines, éventuellement avec irritation par L5—S1 du muscle piriforme — donc une affection neurogène ou neuromusculaire. De plus, la répartition en pourcentage du symptôme de Lasègue est égale chez les hommes et les femmes dans les observations de prolapsus, ce qui n'est pas le cas des observations de malades soumis au traitement ambulant dont les sciatiques doivent être considérées à un degré plus élevé comme étant musculairement conditionnées (tableau 23) — ce qui conduit aussi à considérer ce phénomène comme étant de nature neurogène.

Si les malades sont alors examinés — ils l'ont été à la Clinique par quatre physiurges différents — pour voir si la réaction de Lasègue est positive sans qu'il y ait de modifications musculaires, les observations du prolapsus montrent que 4% ont une réaction positive de Lasègue sans myoses dans la région des fesses, des cuisses et des jambes et que 23% ont + Lasègue sans myoses dans la cuisse et la jambe seulement (tableau 24 A—B). Comme *Helweg*, j'ai fait abstraction des myoses éventuelles dans la région lombaire, de même que je me suis assuré que les malades n'avaient aucune modification radiologique ou déformités du pied. Par contre, 39% n'avaient *pas* la réaction de Lasègue positive, malgré des myoses très prononcées

RECHERCHES

¹ Je remercie vivement le Dr. G. Krogh-Lund, Chef de la Clinique de Rosen-vænget, qui m'a permis de publier ses observations.

Fig. 24 A.

Rapport en p. 100 : + Lasègue avec modifications musculaires palpables :

		p. 100		p. 100		p. 100	p. 100 total
a) D. i. l. IV.	gauche	7	droit	8	bilat.	0	5
b) D. i. l. IV.	gauche	24	droit	28	bilat.	33	28
a) D. i. l. V.	gauche	3	droit	0	bilat.	4	2
b) D. i. l. V.	gauche	20	droit	22	bilat.	8	17

a) en moyenne = 4 %

b) en moyenne = 23 %

a) = + Lasègue ÷ myoses dans les fesses + cuisses et jambes.

b) = + Lasègue ÷ myoses dans les cuisses et jambes seulement.

Fig. 24 B.

Rapport en p. 100 : ÷ Lasègue avec modifications musculaires palpables :

		p. 100		p. 100		p. 100	p. 100 total
a) D. i. l. IV.	gauche	33	droit	32	bilat.	33	33
b) D. i. l. IV.	gauche	0	droit	0	bilat.	0	0
a) D. i. l. V.	gauche	25	droit	56	bilat.	56	46
b) D. i. l. V.	gauche	0	droit	7	bilat.	4	4

a) en moyenne = 39 %

b) en moyenne = 2 %

a) = ÷ Lasègue + myoses dans les fesses + cuisses et jambes.

b) = ÷ Lasègue + myoses dans les cuisses et jambes seulement.

dans la fesse, la cuisse et la jambe, ainsi que 2 % avaient une réaction négative malgré des myoses dans la cuisse et la jambe seulement. Ceci paraît aussi indiquer l'origine neurogène du symptôme de Lasègue.

Si l'on essaie l'opposé du phénomène de Lasègue, on constate dans plusieurs cas de prolapsus de fortes douleurs localisées à l'endroit du prolapsus, à l'hyperextension maximale d'abduction de la hanche; parfois, cette épreuve provoque aussi des douleurs radiculaires caractéristiques. Les malades souffrant de sciatique musculairement conditionnée indiquent très rarement cette douleur comme correspondant à la colonne lombaire — mais plus fréquemment comme partant latéralement de la musculature lombaire. Dans les observations des malades, ce phénomène est souvent désigné comme un symptôme d'hyperlordose (Busch).

Comme déjà mentionné, on trouve des myoses dans les prolapsus des 4^{ème} et 5^{ème} disques intervertébraux dans la même rapport quantitatif et qualitatif que dans les autres lombo-sciatiques; ainsi que le montre la fig. 26, elles sont évidemment plus particulièrement locali-

Fig. 25 A.

Rapport entre les paresthésies et les modifications musculaires palpables :

			p. 100		p. 100		p. 100
D. i. l. IV.	{ + myoses	gauche	11	droit	10	bilat.	12
	{ ÷ myoses	gauche	48	droit	44	bilat.	48
D. i. l. V.	{ + myoses	gauche	25	droit	20	bilat.	7
	{ ÷ myoses	gauche	38	droit	16	bilat.	34

Fig. 25 B.

Rapport entre parésies et modifications musculaires palpables :

			p. 100		p. 100		p. 100
D. i. l. IV.	{ + myoses	gauche	7	droit	8	bilat.	7
	{ ÷ myoses	gauche	19	droit	25	bilat.	21
D. i. l. V.	{ + myoses	gauche	8	droit	8	bilat.	4
	{ ÷ myoses	gauche	10	droit	18	bilat.	16

Fig. 25 C.

Rapport entre atrophie et modifications musculaires palpables :

			p. 100		p. 100		p. 100
D. i. l. IV.	{ + myoses	gauche	11	droit	10	bilat.	8
	{ ÷ myoses	gauche	56	droit	24	bilat.	38
D. i. l. V.	{ + myoses	gauche	20	droit	12	bilat.	4
	{ ÷ myoses	gauche	40	droit	32	bilat.	18

sées dans le côté où siège le prolapsus et indiquent que le malade tend plus les muscles de ce côté pour les soulager.

En ce qui concerne l'autre symptomatologie du symptôme de la sciatique, on a par ailleurs examiné le rapport des paresthésies, des parésies et des atrophies avec les myoses du triceps sural. Ces symptômes neurogènes peuvent apparaître également sans qu'il soit possible de palper de myoses chez les malades (fig. 25 A—C). Si l'on compare le rapport des paresthésies dans nos observations de cas de prolapsus et les observations des malades traités ambulatoirement, on voit que la fréquence des paresthésies est beaucoup plus faible chez ces derniers cas de sciatiques assez récentes, musculairement conditionnées, que chez ceux souffrant de prolapsus chroniques (fig. 23).

Les suédois *Sahlgren*, *Sjöquist* et *Norlén* ont envisagé que la « sensibilité musculaire » comme ils l'appellent, était de nature neurogène étant donné que l'anesthésie de la racine comprimée par le prolapsus

fait disparaître cette sensibilité. Cette « sensibilité » ne doit cependant pas être identifiée aux myoses réelles que l'on observe dans les sciaticques conditionnées par les muscles ou le prolapsus; les myoses ne disparaissent pas à l'anesthésie ou à la narcose; c'est seulement la tension qui entoure la myose qui disparaît. Il n'y a par conséquent aucune raison de croire que les myoses doivent être passées sur le compte des « referred pains » — d'après *Kellgren & Lewis, Brocker et Elliot* — d'autant que tous les muscles affectés ne correspondent pas aux racines comprimées.

Dans un examen tel que celui auquel il a été procédé ici, il peut y avoir un certain intérêt à savoir combien de prolapsus discaux on rencontre dans un matériel d'observation *non* sélectionné — c'est-à-dire parmi des cas de lombo-sciaticques *non* hospitalisés, mais traités ambulatoirement; *Torben Andersen* prétend que dans 90% des cas de « sciaticques idiopathiques » il a trouvé des traces de maladies intrarachidiennes; *Boland & Corr* ont trouvé 7,1% chez 181 cas de maladies dorsales hospitalisées, *Steinbrocher* et *Comroe* estiment que 2 à 4% est la moyenne obtenue pour les cas analysés dans leur hôpital. Les observations de malades traités ambulatoirement par la Clinique des Caisses de Maladies, que j'ai citée plus haut, montrent que 4 à 5 p.100 ont été soupçonnés de prolapsus, dont 2 envoyés à l'hôpital. Dans l'analyse de la fréquence, il faut donc distinguer minutieusement entre les cas chroniques des hôpitaux et les cas récents traités ambulatoirement — autrement le problème apparaît sous un angle erroné pour les médecins praticiens.

Etant donné que dans les cas récents de prolapsus discaux lombaires il ne se manifeste pas des symptômes typiquement différents des autres cas de lombo-sciaticques, il y a lieu d'appliquer à tout malade présentant des symptômes de sciaticques dans la région lombaire, les fesses et les membres inférieurs, un *traitement physiurgique suffisant* — en appuyant sur chacun de ces deux derniers mots — pendant une période allant *jusqu'à* deux mois. Si l'on constate des parésies ou/et des troubles sphinctériens, le malade doit être immédiatement hospitalisé.

Si le traitement n'aide pas, le diagnostic de la sciaticque musculairement conditionnée doit être remis en discussion et toutes les maladies pouvant causer des douleurs sciaticques secondaires prises en considération, dans le cas où ces affections primaires n'ont pas déjà été découvertes au cours des premiers mois d'examen et de traitement.

La *conclusion* de l'examen physiurgique c'est que les symptômes d'abolition neurogènes doivent être considérés comme la conséquence de la compression exercée par le prolapsus sur les racines et ne sont

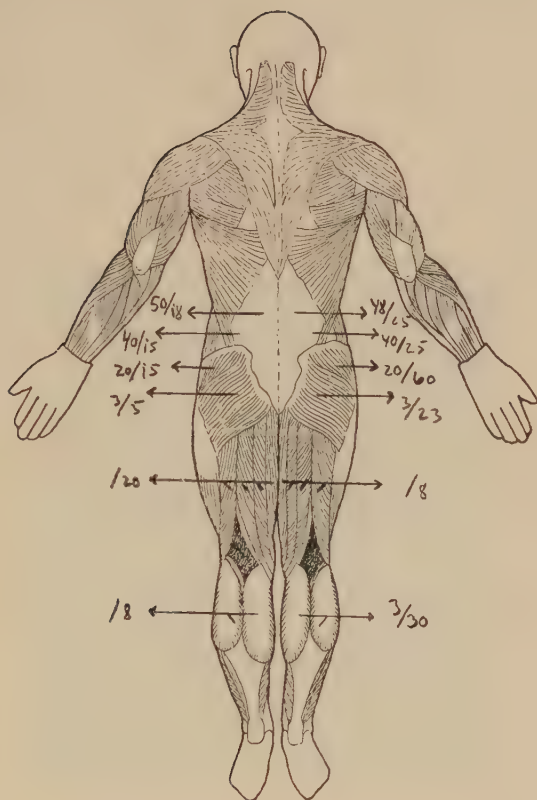


Fig. 26.

Répartition en p. 100 de myosites diffuses et localisées chez des malades souffrant de prolapsus du côté droit du 4ème disque intervertébral lombaire. (50/18 = degré de consistance de la répartition diffuse /localisée).

pas musculairement conditionnés — de même que les myosites sont de nature *secondaire*, nées de la statique et de la fonction modifiées par les douleurs. C'est pourquoi les myosites ne peuvent pas contribuer à établir le diagnostic du prolapsus, voire à déterminer le niveau du siège du prolapsus.

Le prolapsus discal lombaire doit être considéré comme une cause étiologique du syndrome de la lombo-sciatique qu'il faut envisager lorsqu'un *traitement physiurgique suffisant* n'apporte aucune amélioration au cours d'une période raisonnable.

MYÉLOGRAPHIE — INDICATION DE L'OPÉRATION — OPÉRATION

Par EDUARD BUSCH

Myélographie.

Ce qui a été dit plus haut montre clairement que dans la plupart des cas, sur la base notamment de la localisation de la douleur radiculaire et des symptômes d'abolition neurogènes, nous pouvons établir le diagnostic purement clinique du prolapsus discal lombaire et que, par ailleurs, nous sommes assez bien renseignés sur le siège du prolapsus. Au tableau reproduit à la fig. 27, on verra toutefois l'énorme

Fig. 27.

<i>Incidence de la myélographie pour les malades Nos 1 à 400.</i>	
Myélographie à l'huile iodée, chez nous	9 %
" " dans d'autres services	3 %
Myélographie à l'oxygène, chez nous	47 %
" " dans d'autres services	34 %
Myélographies épidurales	5 %
Opération directe sans myélographie	5 %
<i>Incidence de la myélographie pour les malades Nos. 901 à 1000.</i>	
Myélographie à l'oxygène, chez nous	0 %
" " dans d'autres services	15 %
Myélographie à l'abrodil, chez nous	0 %
" " dans d'autres services	9 %
Myélographie au pantopaque, chez nous	6 %
" " dans d'autres services	10 %
Opération directe sans myélographie	60 %

changement apporté par l'expérience acquise en comparant la fréquence de la myélographie chez nos 400 premiers malades et chez nos derniers 100 malades. Tandis que l'on procédait autrefois à la myélographie sous une forme ou l'autre, on ne l'utilise maintenant qu'à titre exceptionnel et elle n'est nécessaire que dans 10% environ des cas de malades directement hospitalisés dans un service de neurochirurgie. Mais chez ces 10%, de même que chez les malades hospitalisés sans qu'ils présentent des symptômes typiques et chez lesquels l'examen ne révèle pas non plus de prolapsus, la myélographie est toujours nécessaire. Alors que nous avons abandonné la *myélographie à l'iode*, lipiodol ou immetal, dès que notre technique opérative fit que nous n'avons plus ouvert la dure-mère de manière à pouvoir éliminer le contrastant, nous avons continué pendant un certain temps à pratiquer la *myélographie à l'oxygène* surtout après avoir découvert qu'il fallait donner une certaine surpression à l'air injecté. Même si l'on

s'en tient strictement aux directives — ce qui n'a pas toujours été le cas — cet examen est cependant fort désagréable pour les malades et il arrive par ailleurs souvent qu'il ne donne pas le résultat espéré, surtout lorsqu'il s'agit du 5^{ème} disque chez des malades corpulents. Les essais avec le *contrastant épidual* ont montré que ces examens étaient peu sûrs, mais nous n'avons jamais voulu utiliser la *myélo-*



Fig. 28.

Prolapsus discal médian à la myélographie au pantopaque. De petits prolapsus latéraux n'apparaissent pas sur le myélogramme.

graphie à l'abrodil. En effet, l'abrodil irrite les racines rachidiennes à tel point qu'il est nécessaire de pratiquer l'anesthésie rachidienne avec tous les dangers de complications médullaires qu'elle comporte (13% sur 2493 cas (*Thorsen*)). Ces dernières années, lorsqu'il a été nécessaire de pratiquer un examen au moyen d'un contrastant, nous avons utilisé la myélographie au pantopaque (fig. 28). Le pantopaque est si liquide qu'on peut, une fois l'examen terminé, en appliquant la technique voulue, le sucer totalement ou presque entièrement avec la seringue, mais il est indispensable d'avoir pour cela une certaine pratique. Cet examen semble être aussi sûr que la myélographie à l'iode et nous n'avons pas constaté d'inconvénients sérieux (un travail plus approfondi sera d'ailleurs publié prochainement par notre service à ce sujet). Cet examen nous paraît être le meilleur quand il est

nécessaire d'avoir recours à la myélographie dans les cas de prolapsus discaux, mais dans la plupart des cas nous préférons nous en passer. Si le diagnostic du niveau du prolapsus n'est pas absolument certain, nous faisons tout d'abord une hémilaminectomie partielle du disque suspect et si le prolapsus ne s'y trouve pas nous pratiquons une hémilaminectomie partielle du disque suivant puisqu'il s'agit presque toujours du 4^{ème} ou du 5^{ème} disque.

Indication de l'opération. Si nous avons trouvé que le malade souffre d'un prolapsus discal, cela signifie-t-il toujours que l'opération soit indiquée ? A notre avis pas forcément : beaucoup de prolapsus discaux revenant à l'état latent d'eux-mêmes ou à la suite d'un traitement physiurgique approprié. Ils peuvent laisser une certaine raideur dans la région lombaire, provoquer de légères douleurs et, à plusieurs années d'intervalles, des sciatiques isolées, mais au fur et à mesure que le prolapsus s'installe dans le canal rachidien où il ne comprime pas les racines, le malade retrouve le calme. Nous avons peut-être été quelque peu sévères dans les indications de nos opérations, mais nous maintenons toujours que nous n'opérons pas les malades à la première attaque ou avant qu'un traitement conservateur ait été essayé sans résultat, pendant une période suffisamment longue. Il y a peu d'exceptions à cette règle — et il s'agit essentiellement de *prolapsus au cours continu* (fig. 5) où les parésies et les troubles de la sensibilité s'accroissent constamment et où l'opération est aussi absolument indiquée que lorsqu'il s'agit d'une tumeur, les parésies radiculaires ayant un pronostic défavorable avec très lente restitution. Pour les autres malades, l'indication de l'opération doit toujours être individuelle. Lorsque les crises récidivent et que le travail du malade ne lui permet pas de se ménager, on sera enclin à l'opération, en tenant évidemment toujours compte de l'âge et de l'état psychique du malade. Il n'y a pas de doute non plus en ce qui concerne les malades chez lesquels les intervalles entre les attaques de douleurs sont si courts que la maladie désorganise entièrement la vie et le travail du malade. La décision doit être prise ici, comme d'ailleurs pour toutes les interventions chirurgicales, en considérant l'importance prise par la maladie dans la vie de chaque malade en particulier.

Opération. L'opération a pour but d'extirper le prolapsus sans endommager les structures environnantes. Un prolapsus discal est une affection située assez profondément où la mise à nu joue un rôle important. Les premiers temps, nous mettions le prolapsus à nu comme une tumeur par *laminectomie* de deux, plus tard d'une vertèbre, après quoi nous avons passé à l'hémilaminectomie remplacée ensuite par l'*hémilaminectomie partielle* où l'on n'enlève qu'une petite partie



Fig. 29.

Le prolapsus discal est mis à nu (hémilaminectomie partielle) et on le voit apparaître juste au bout de l'instrument.

du bord de l'os; quelques opérateurs ont dans un certain nombre de cas opérés *transligamentairement* à travers le ligament jaune, n'enlevant aucune partie osseuse. Cette dernière technique est évidemment l'idéale, mais elle demande une grande pratique et les résultats ne semblent guère meilleurs qu'avec l'hémilaminectomie partielle. La nécessité de former constamment de nouveaux opérateurs fait cependant que l'on procède toujours aussi bien à l'hémi qu'à la laminectomie. L'essentiel est de ne pas endommager et il est plus facile de voir l'ensemble des faits par les procédés de mise à nu employés d'abord. Les premières années, nous n'enlevions que le tissu formant le prolapsus, mais devant la possibilité de récédive, nous avons vite été amenés à enlever tout le tissu pulposus se trouvant dans le disque — bien entendu sans fanatisme — et c'est devenu la règle depuis dix ans.



Fig. 30.

Le prolapsus libéré est dégagé — tenu dans la pince.

Nous avons rarement procédé à des opérations de fixation de la colonne — il s'agit seulement de 4 malades au dos très peu stable. Nous considérons que notre mission est d'enlever le prolapsus, supprimant par là la compression des racines rachidiennes qu'il entraîne et, comme on le verra par la suite — cela s'est avéré suffisant dans la plupart des cas. A notre avis une ostéosynthèse n'a de valeur que dans moins de 10% des cas et elle est mieux réalisée plus tard dans un service d'orthopédie — si on estime qu'elle est indispensable. D'après nous, il n'y a aucune raison de pratiquer des opérations de fixation à l'avantage de cette minorité, en imposant à tous les autres malades une convalescence de plusieurs mois.

Les sutures sont retirées le 8^{ème} jour. Le 9^{ème} jour le malade est assis dans son lit, le 10^{ème} jour il est levé et assis sur une chaise, le 11^{ème} jour on l'autorise à aller du lit à la chaise, le 12^{ème} jour il sort dans le corridor, le 13^{ème} jour il fait le tour de la maison et il rentre

Fig. 31.

Séjour à l'hôpital post-opératoire (340 malades).

Jusqu'à 15 jours	142 malades, soit 41 %	} 71 %
" 20 " 	105 " soit 30 %	
" 30 " 	50 "	
" 40 " 	14 "	
" 50 " 	9 "	
" 60 " 	8 "	
" 70 " 	5 "	
" 80 " 	3 "	
" 90 " 	4 "	

Les séjours de 21 à 40 jours sont dus principalement aux douleurs (28) et hématome (réopération 8).

Les séjours dépassant 40 jours sont dus essentiellement à des infections (7), parésies préopératives (8), phlébites (4), pneumonies (2).

chez lui ce jour-là ou le jour suivant. On lui donne des instructions détaillées sur la manière dont il doit ménager son dos pendant le premier mois, éviter de soulever et de travailler durement pendant les deux premiers mois — tout cela à condition que le cours de la maladie évolue normalement et que le malade ne ressente pas de douleurs, ce qui a été le cas de plus des $\frac{2}{3}$ de nos premiers 300 malades (fig. 31). Il nous est impossible d'indiquer des données chiffrées pour nos autres malades, le manque de place dans notre service ayant fait que nous avons généralement été obligés de renvoyer les malades dans un autre hôpital 3 à 4 jours après l'opération, à notre et à leur grand regret. Durant certaines périodes, nous avons procédé à des essais d'alitement plus long appliqué notamment par les américains, mais d'après nos observations il ne semble pas qu'une plus longue durée d'alitement du malade joue un rôle pour le résultat définitif, à condition que le malade n'ait pas de douleur. Il est sans doute nécessaire de le garder couché s'il en a. Les douleurs dans la période post-opératoire peuvent être dues au fait que le prolapsus n'a pas été entièrement extirpé, à une contusion de la racine rachidienne au cours de l'opération ou — le plus souvent — à des modifications massives physiurgiques des parties molles qui peuvent subsister pendant quelque temps après l'enlèvement du prolapsus. Dans ce dernier cas, on peut avoir recours à la diathermie, à un massage *léger* et à des exercices d'attitude. Comme les américains, nous avons parfois utilisé le corset d'étoffe au début et c'est peut-être une bonne idée — non pas parce que le corset soutient beaucoup, mais parce qu'il rappelle constamment au malade qu'il doit ménager son dos.

ANATOMIE PATHOLOGIQUE

Par ERNA CHRISTENSEN

Le disque intervertébral est formé de fibrocartilage qui, en raison de sa structure peut être divisé en une partie périphérique, l'annulus, avec des fibrilles serrées disposées comme des lamelles et des cellules cartilagineuses disséminées, isolées ou en petits amas — et le tissu central pulposus dont la structure est indécise avec un cours irrégulier des fibrilles et, en général, plusieurs cellules cartilagineuses formant



Fig. 32.
Prolapsus typique.

un amas plus gros. Le tissu de l'annulus se poursuit dans la plaque cartilagineuse hyaline dans la partie adjacente de la vertèbre, tandis que sur les côtés elle forme la partie extérieure du disque. La plaque cartilagineuse hyaline est riche en cellules et les cellules cartilagineuses sont disposées en colonnes.

Le disque ne se forme définitivement que pendant la croissance et il se modifie normalement au cours des années, de sorte que le pulposus contient plus d'eau et est moins ferme pendant l'enfance que plus tard. Dans l'ensemble, il se produit une atrophie universelle du disque, celui-ci devenant plus bas. Par ailleurs, il peut se produire des fissures dans l'annulus et le pulposus provenant de dégénéralions ressemblant aux muqueuses. D'après Schmorl, le tissu du disque est si hautement différencié qu'il ne peut être régénéré et c'est pourquoi la guérison après les ruptures ne peut se faire que par la croissance du tissu de granulation environnant et par la transformation secondaire de celui-ci en tissu connectif fibreux qui se calcifie ou s'ossifie plus tard (voir *Malmros*).

Au point de vue macroscopique, le prolapsus se présente (fig. 32) comme un renflement polypeux ou papillomateux de grandeur variable situé extraduralement, au niveau du disque intervertébral. Souvent on voit aussi un renflement grisâtre de l'arachnoïde autour des racines qui passent juste au-dessus du disque.

Le prolapsus lui-même est blanc, un peu brillant, filandreux, sans capsule démontrable macroscopiquement, mais avec un tissu périphérique plus ferme.

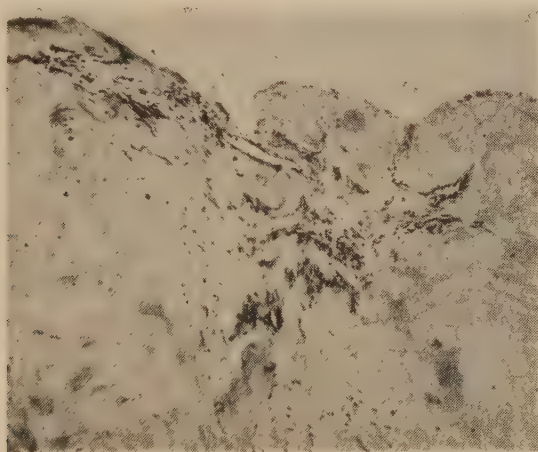


Fig. 33.

Microphoto d'un prolapsus discal avec infiltration de cellules rondes.

Parmi les premiers 400 malades opérés pour prolapsus discal lombaire dans le Service de Neurochirurgie de l'Hôpital de l'Université, il a été procédé à la microscopie pour 393. Chez 28 de ces malades le prolapsus discal a été extirpé en un morceau. Chez les autres 365, il a été enlevé par morceaux plus ou moins grands. Tout le tissu extirpé a été envoyé à la microscopie, également la partie du nucléus pulposus éliminée en vidant le disque et ne faisant pas partie du prolapsus. L'examen histologique donne des indications sur les modifications dégénératives dans le prolapsus et le tissu discal dans son ensemble.

Comme il fallait s'y attendre, il y avait du tissu pulposus dans la plupart des cas, à savoir chez 351, soit 88%, tandis que l'on a trouvé du tissu annulus chez 296 (74%). Un certain nombre de ceux-ci doivent sans doute être comptés comme appartenant au tissu annulus

se trouvant immédiatement contre le prolapsus discal ou représentant la partie de l'endroit où s'est produite la rupture du tissu annulus.

L'examen microscopique n'a pas démontré non plus de capsule entourant le prolapsus. Par contre, on voit fréquemment le long de la surface polypeuse, effilochée et le long des ruptures à l'intérieur du prolapsus, des dépôts de fibroblastes, lymphocytes, macrophages et dans certains cas de plasmacellules. Cette infiltration de cellules rondes a été observée chez 124 malades (31%). Chez 55, ou 16% au total parmi ceux-ci, on a par ailleurs démontré du tissu de granulation de différents âges. Enfin, chez deux on voit une croissance de vaisseaux dans le tissu fibreux du prolapsus.

Même si le tissu de granulation est d'âge différent, il ne peut être démontré de parallélisme entre l'âge du prolapsus discal et celui du tissu de granulation, ce qui provient vraisemblablement du fait que le premier ne se forme que peu à peu, sans doute après une série de nouveaux petits traumatismes. Par ailleurs, comme mentionné plus haut, le tissu de granulation semble croître de l'extérieur vers l'intérieur, étant donné qu'il n'y a pas de vaisseaux dans le tissu du disque et il faut donc qu'il y ait un dépôt du prolapsus discal contre le tissu paravertébral contenant des vaisseaux, par ex. le tissu épidural graisseux.

On aurait sans doute trouvé encore plus de tissu de granulation dans un plus grand nombre de prolapsus si ceux-ci avaient été préparés en séries de coupes.

Dans un certain nombre de prolapsus le tissu a été le siège d'une certaine transformation fibreuse, mais il est difficile de la chiffrer exactement, une estimation se basant toujours sur une appréciation et le tissu discal changeant normalement d'aspect avec l'âge.

Chez 21 (5% des malades), il y a ossification ou métaplasie osseuse. Chez certains cependant elle n'en était encore qu'à la formation de tissu ostéoïde. Dans la plupart des cas, il s'agit toutefois de tissu osseux riche en cellules, bien formé, se trouvant à l'intérieur du prolapsus discal, ce qui fait qu'il est impossible de le confondre avec le tissu osseux de la vertèbre ou de l'arc.

Dans 3 cas on a trouvé un dépôt de chaux sans formation d'os.

Enfin, chez 4 malades il restait des traces d'un ancien épanchement de sang dans le prolapsus discal apparaissant sous forme de macrophages avec pigments sanguins et des pigments sanguins libres causés vraisemblablement par une hémorragie dans le tissu de granulation existant, à la suite de petits traumatismes dans un prolapsus discal déjà existant avec tissu de granulation.

Les infiltrations de cellules rondes doivent être considérées de

même que le tissu de granulation comme un phénomène réactif dans les processus dégénératifs du prolapsus discal et sont peut-être les avant-coureurs du tissu de granulation qui est suivi lui-même de la transformation fibreuse, éventuellement de la métaplasie osseuse du prolapsus.

RÉSULTATS DU TRAITEMENT

Par EDUARD BUSCH

Un des axiomes préférés de *Harvey Cushing* était : « *The proof of the pudding is in the eating* ». En conséquence, quels ont été pour les malades le résultat de nos travaux sur le prolapsus discal lombaire ? La réponse à cette question est fournie par le tableau reproduit à la fig. 34 qui donne le résultat des examens complémentaires de nos premiers 800 malades. Nous avons réexaminé un certain nombre de ces malades dans notre service, tandis que nous nous sommes contentés d'envoyer des questionnaires à ceux dont le domicile est éloigné de Copenhague. Il convient de souligner à cet égard qu'il faut tenir compte de la politesse et de l'amabilité des malades à l'égard du Service d'Hôpital qui procède à une enquête de ce genre. Nous avons essayé d'éliminer ce facteur en demandant toujours expressément si, après l'opération, le malade a consulté un médecin ou a été hospitalisé et, dans l'affirmative, nous avons écrit au médecin ou à l'hôpital en leur

Fig. 34.

Réexamination de 800 malades opérés pour prolapsus discal lombaire.

Période écoulée depuis l'opération	I	II	III	IV	Nombre
1 à 2 ans	133	37	15	8	193
2 à 3 ans	93	41	8	0	142
3 à 4 ans	64	14	10	2	90
4 à 5 ans	94	21	9	5	129
5 à 6 ans	62	9	6	2	79
6 à 7 ans	56	8	5	1	70
7 à 8 ans	22	5	3	1	31
8 à 9 ans	15	1	1	0	17
9 à 10 ans	3	2	0	0	5
plus de 10 ans	1	0	0	1	2
	543	138	57	20	758
	67,9 %	17,3 %	7,1 %	2,5 %	

+ 4 décès post-opératoires (0,5 %). 4 malades sont décédés pour des causes irrelevantes pendant la période d'observation, tandis qu'il a été impossible de retrouver 34 malades (4,3 %).

Groupe I = bien portants, entière capacité de travail : $543/758 = 72\%$.

Groupe II = soulagement partiel (voir texte), aptes au travail : $138/758 = 18\%$.

Groupe III = soulagement partiel, partiellement aptes au travail : $57/758 = 8\%$.

Groupe IV = ni amélioré, ni empiré, incapables de travailler : $20/758 = 3\%$.

demandant des renseignements sur l'état du malade; dans la grande majorité des cas ces indications concordaient avec celles données par le malade lui-même. Nous avons réparti les malades réexaminés en quatre groupes : Groupe I, guéris, aptes au travail, Groupe II, malades ayant eu quelques accès de douleurs, mais qui dans l'ensemble peuvent travailler et se portent bien ou malades ayant toujours des symptômes non invalidisants, en particulier des paresthésies, de légères douleurs lombaires, etc., Groupe III, malades n'étant que partiellement aptes au travail à cause des douleurs, parésies, paresthésies ou neuroses, et ne pouvant fournir qu'un travail facile, Groupe IV, incapables de travailler. Nous voyons ainsi que plus des $\frac{2}{3}$ des malades ont eu un bon résultat et que l'état de 17% s'est trouvé amélioré. Par rapport à la période qui s'est écoulée, il semble que l'enquête effectuée puisse donner des résultats à peu près sûrs, le groupe le plus ancien et le plus important ayant ainsi une période d'observation de 6 ans.

Mais il n'y a pas lieu de s'arrêter plus longuement sur les *bons* résultats, bien que ce soit évidemment un grand encouragement de rencontrer la reconnaissance des malades au cours des examens complémentaires. Si nous voulons aller de l'avant, c'est sur les *mauvais* résultats que doit se porter notre attention. En tout premier lieu sur la *mortalité des opérations*, soit 4 malades — c'est-à-dire 0,5% de nos premiers 800 malades (plus tard nous en avons encore opéré 400 sans décès, de sorte que le taux effectif de mortalité sur 1200 malades a été de 0,3%). Les quatre décès ont été dus respectivement à une embolie pulmonaire, une dilatation cardiaque aiguë, une coronarthrombose et une infection. Dans les observations chirurgicales, il y a toujours une certaine mortalité et celle-ci ne nous semble pas être prohibitive, bien qu'elle souligne la vieille règle de la chirurgie qui est de ne pas opérer si on peut l'éviter — c'est-à-dire que le malade doit être incapable de travailler ou sa vie troublée par les douleurs, les alitement réitérés, etc. (voir sous indication de l'opération, p. 486). Et il ne faut jamais oublier que cette mortalité, qui tient si peu de place au point de vue statistique, est une affaire très grave pour la famille qu'elle touche et pour le médecin traitant, surtout s'il s'agit d'une maladie qui ne comportait pas en soi un danger vital.

En ce qui concerne les autres résultats défavorables, nous nous sommes efforcés d'hospitaliser tous les malades présentant des symptômes post-opératoires afin d'en rechercher la cause. Parmi ceux-ci 10 souffraient d'un *prolapsus dans un autre disque* et c'est pourquoi au cours des dernières années, nous explorons également le 5^{ème} disque si nous trouvons un prolapsus dans le 4^{ème} disque et vice versa. Comme indiqué à la p. 486 ceci a donné des résultats puisque nous trouvons

maintenant beaucoup plus de prolapsus multiples qu'au cours des premières années où nous n'y faisons pas attention. Parmi les malades réopérés, il n'y a eu aucune manifestation de symptômes chez 8 après la 2^{ème} opération, tandis que 2 appartiennent au groupe II. Chez 7 malades réhospitalisés, on a constaté une *récidive* du prolapsus du disque déjà opéré; ces cas datent des premières années où nous ne vidions pas le disque aussi minutieusement que maintenant. Parmi ces 7 malades, aucun symptôme ne s'est manifesté après la 2^{ème} opération chez 4, deux rentrent dans le groupe II, un dans le groupe III. A la deuxième hospitalisation, on a découvert que 26 malades souffraient seulement de *myoses* ou d'autres douleurs musculaires; la plupart d'entre eux sont revenus assez peu de temps après l'opération et se sont rapidement améliorés après un traitement physiurgique compétent. Chez 7 des malades réopérés, on n'a trouvé que des racines rachidiennes enflées, injectées — la *radiculite* que nous avons souvent constatée dans les cas anciens, lorsque, les premières années, nous ouvrons le sac dural. Les racines peuvent être littéralement fixées à la dure-mère au-dessus du prolapsus saillant ou, en cas de réopération, à l'endroit où se trouvait antérieurement le prolapsus. Chez ces malades, nous nous sommes bornés dans 4 cas à détacher les racines, tandis que dans 3 où une seule racine était adhérente, nous avons procédé à la rhizotomie de la racine. Les résultats ont été à peu près bons, mais il semble que les malades mettent près d'un an à se rétablir complètement — nos cas ont d'ailleurs presque toujours été réopérés dans le cours de l'année qui a suivi la première opération.

Un petit groupe de malades se plaignent de *lumbago* et de sensations de faiblesse dans la région lombaire. Le corset d'étoffe peut parfois aider le malade pendant la première période, jusqu'à ce que la stabilité soit rétablie, mais chez d'autres (voir p. 486), il est nécessaire de pratiquer une opération stabilisante qui, selon nous, doit être faite secondairement, quand elle s'avère nécessaire. Chez 3 de nos malades nous avons ainsi secondairement pratiqué l'opération d'Albee ou une opération similaire, mais il est encore trop tôt pour se prononcer sur ses effets.

Fig. 35.

Méthodes opératoires.

Hémilaminectomie partielle	438
Hémilaminectomie sur deux pédicules	312
Laminectomie	179
Opération transligamentaire	71

Tandis que les groupes mentionnés jusqu'à présent ne donnent lieu à aucune inquiétude sérieuse, la chose est toute différente pour les autres groupes : il a fallu réopérer 16 malades pour ce que nous appelons la *compression cicatricielle de la racine* — à la réopération on trouve le champ de la première opération recouvert d'un tissu cicatriciel ferme, presque cheloïde (fig. 36) qui fixe les racines. Chez 10 de ces malades nous avons procédé à la rhizotomie d'une ou de

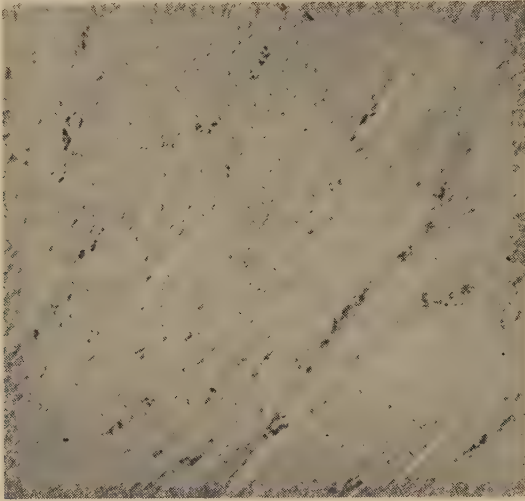


Fig. 36.

Tissu connectif compact dans les cas de compression cicatricielle de la racine.

deux racines postérieures, mais ce traitement ne nous a pas semblé convaincant; il en est de même de l'enlèvement laborieux du tissu cicatriciel — on a l'impression qu'il va se reformer. Nous ne savons rien de certain sur la cause de cette compression du tissu cicatriciel, mais il semble qu'elle se produise notamment dans les cas où il y a eu des hémorragies de veines épidurales pendant l'opération et il est certain qu'elle apparaît le plus souvent pour les opérateurs peu exercés. Si les malades de ce groupe se guérissent néanmoins, c'est sans doute parce que le tissu cicatriciel se vascularise peu à peu. Plusieurs malades ont été traités aux rayons X dans l'espoir que ce traitement entraînerait la formation de tissu conjonctif, mais nous ne savons pas encore quel en a été l'effet. Dans les cas désespérés, on peut évidemment recourir à la chordotomie, et il est possible que nous ayons été trop réservés vis à vis de cette intervention — lorsque le malade est si atteint, il est

généralement si neurotique que l'on ne peut autrement guère s'attendre à un bon résultat. Une *neurose* peut évidemment aussi pour d'autres raisons, compromettre les résultats.

Nous avons essayé de considérer nos résultats de traitement, bons et mauvais, par rapport à différents faits : tout d'abord en les rapprochant de l'âge des malades, et il apparaît que les résultats sont nettement meilleurs chez les malades opérés avant l'âge de 40 ans. Ensuite, de la *durée de l'anamnèse* où il y a une légère augmentation du nombre de mauvais résultats dans les cas présentant de longues anamnèses. D'autre part, du *disque*, afin de voir si l'on obtient de meilleurs résultats dans les prolapsus discaux du 4^{ème} ou du 5^{ème} disque lombaire, bien que les chiffres soient indiscutablement trop bas pour pouvoir donner une sécurité absolue. Par ailleurs, on pourrait penser que la mise à nu joue un rôle et que l'on pourrait constater chez les malades laminectomés de plus gros inconvénients post- opératoires que chez ceux auxquels il n'a été pratiqué qu'une hémilaminectomie ou une opération transligamentaire, ce qui ne semble toutefois pas être le cas, bien qu'il y ait une petite différence, pas très sûre, à l'avantage des hémilaminectomies. C'est probablement le hasard qui a voulu qu'aucun des malades *transligamentairement* opérés n'est rangé dans un groupe inférieur au groupe II. L'application de cette technique dépend de la pratique de l'opérateur qui joue ici un rôle très important : le tableau de la fig. 37 a placé les résultats du traitement obtenus par cinq opérateurs dont

Fig. 37.

Résultats et expérience du chirurgien.

(A a opéré 6 fois autant de cas de prolapsus discal que F).

	A	B	C	D	E	F
Bons résultats en p. 100	86	80	75	70	67	55
(groupes I et II)						

l'expérience était variable et l'on constate une différence marquée à l'avantage des opérateurs qui ont pratiqué le plus grand nombre d'interventions, ce qui ne peut guère surprendre, mais ce qui signifie cependant que l'on ne doit pas pratiquer l'opération du prolapsus discal si l'on n'a pas un certain nombre de cas par année. Par contre, en suivant les directives décrites ici, on peut escompter que l'opération rendra à la majorité des nombreux malades incapables de travailler par suite d'un prolapsus leur capacité de travail et supprimera leurs symptômes.

REMARQUES FINALES

Tandis que dans les travaux qui précèdent, nous nous sommes occupés de prolapsus discaux *vérifiés* et avons essayé de rendre compte

des faits chez les malades dont la cause de la maladie est connue, nous allons pour terminer mentionner sommairement la signification des maladies du prolapsus pour notre compréhension de l'ensemble du problème de la sciatique. Nos observations ne sont évidemment pas de nature à décider quelle est la part du problème de la sciatique qui se trouve résolue par la constatation du prolapsus discal lombaire, puisque de par sa nature même, il est fortement filtré de prolapsus dont le pourcentage est très élevé. Alors qu'à l'origine nous étions un peu sceptiques à l'égard de *Torben Andersen* qui soulignait la fréquence des processus intrarachidiens et notamment du prolapsus discal dans les cas de sciatique des Services de Médecine des hôpitaux (> 90% positifs à la myélographie), les expériences que nous avons faites plus tard semblent indiscutablement indiquer que le prolapsus discal lombaire est bien la cause la plus fréquente de la « sciatique » typique de caractère radiculaire — en tout cas pour ce qui est des « sciatiques » que l'on voit dans les hôpitaux. Pour le médecin praticien la situation est sûrement différente — il se trouve en face de malades souffrant de sciatiques que nous ne voyons jamais dans les hôpitaux, parce qu'ils se guérissent après une certaine période d'alitement et de traitement à la maison. Il peut s'agir ici de modifications purement musculaires causées par une surcharge de l'organisme, des traumatismes ou du rhumatisme. Un certain nombre de ces malades souffrent toutefois — comme le montrent nos anamnèses — d'une compression radiculaire par suite des prolapsus, spontanément supprimée par un des moyens mentionnés plus haut. D'autres parmi ces malades — *la plupart* d'entre eux — auront encore quelques attaques au cours des années suivantes, mais celles-ci deviennent de plus en plus rares et cessent au fur et à mesure qu'un prolapsus incomplet se déshydrate ou qu'un prolapsus complet s'adapte à la place existant dans le canal rachidien. Il ne reste alors qu'une raideur plus ou moins marquée dans la colonne lombaire à la suite d'une modification du disque, tandis que le prolapsus lui-même est asymptomatique. A notre avis, il n'y a guère de doute que la physiurgie moderne avec ses exercices d'attitude et son enseignement des positions correctes de travail, comme relevé en particulier par *Helweg* et *Svend Clemmensen* peut aider beaucoup de ces malades vers une telle évolution. D'autres malades — *le plus petit nombre* — auront des attaques intermittentes toujours croissantes et devront alors être opérés lorsque la situation devient intenable, mais *avant* que les symptômes d'abolition neurologiques sérieux soient devenus irréparables. Dans la grande minorité des cas, il se manifestera rapidement des symptômes graves et les malades en question doivent être opérés immédiatement. Il faut souligner en outre que l'indication de l'opération est la *com-*

pression radiculaire avec symptômes d'irritation et d'abolition, tandis que l'extirpation du prolapsus ne rend pas le disque lombaire rompu normal. Chez la plupart des malades opérés, la colonne se stabilise comme chez les non-opérés mentionnés ci-dessus, mais il peut être question de pratiquer une stabilisation orthopédique chez certains d'entre eux.

Nous estimons avoir la preuve que l'on obtient des résultats satisfaisants si l'on envisage de cette manière le « problème de la sciatique ».

Si nous essayons maintenant de *résumer* les enseignements que nous avons tirés de notre travail sur le prolapsus discal lombaire, nous arrivons aux conclusions suivantes :

1. Le prolapsus discal lombaire est une affection fréquente et peut-être la maladie que cause le plus grand nombre de cas des lombosciatiques avec symptômes d'irritation radiculaire ou symptômes d'abolition.
2. Parmi 1000 cas de prolapsus discaux lombaires vérifiés, de loin la plus grande partie étaient localisés dans le 4^{ème} ou le 5^{ème} disque (respectivement 50,8 et 41,3 %). Les prolapsus peuvent être multiples.
3. Le dur travail physique et les traumatismes jouent un rôle dans l'évolution — c'est ainsi que chez plus de la moitié des malades on a pu retrouver un traumatisme causal probable.
4. Le prolapsus et sa localisation peuvent être diagnostiqués dans la plus grande majorité des cas par la radiographie ordinaire et l'examen clinique, la myélographie (de préférence au pantopaque) n'étant nécessaire que dans 10 % des cas.
5. L'opération n'est nécessaire que dans une petite minorité des cas de prolapsus discaux lombaires. L'indication de l'opération dépend du rôle que jouent la maladie et ses symptômes dans la vie du malade. Si cependant il y a des signes objectifs de symptômes radiculaires d'abolition (troubles de la sensibilité et parésies) qui ne disparaissent pas rapidement, l'opération sera souvent indiquée; elle l'est absolument lorsqu'il y a des symptômes de compression étendue ou de bloc rachidien.
6. Avec les indications et la technique appliquées ici, on obtient de bons résultats à l'opération chez plus de 70 %, une amélioration chez 18 %, tandis que les résultats sont directement peu satisfaisants chez plus de 10 % (758 réexaminés).
7. Les mauvais résultats sont dus essentiellement aux faits suivants : compression cicatricielle de la racine, radiculite, instabilité du disque malade, myoses et neurose.

LITTÉRATURE

Sur l'abondante littérature publiée, nous nous bornons à renvoyer à quelques monographies importantes qui donnent une liste complète de la littérature: *F. Keith Bradford & R. Glenn Spurling* : Le disque intervertébral (2ème édition 1945 (C. C. Thomas)), *R. Malmros* : Le prolapsus discal lombaire et la compression ligamentaire des racines (Copenhague 1942), *G. Norlén* : Valeur des symptômes neurologiques dans la sciatique pour la localisation de la hernie discale lombaire (Acta Chir. Scand. suppl. 95, Stockholm 1944), une liste plus complète pouvant par ailleurs être fournie par les auteurs.

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